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#### **DESCRIPTION**

# PLASMODIUM FALCIPARUM ANTIGENS AND METHODS OF USE

The subject invention was made with government support under a research project supported by Grant No. 1 R43AI49051-01 NIAID.

## Cross Reference to Related Application

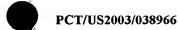
[0001] This application claims the benefit of U.S. Provisional Application 60/431,494, filed December 6, 2002, which is hereby incorporated by reference in its entirety, including all drawings and tables.

#### **Background of Invention**

[0002] The recent explosion in genomic sequencing has deposited a wealth of information in the hands of researchers. However, there is not yet a means to efficiently analyze such data to identify which antigens among many thousands are appropriate targets for vaccine development.

[0003] More than 5000 proteins are expressed during the life cycle of the *Plasmodium* spp. parasite. Subunit vaccines currently in development are based on a single or few antigens and may therefore, elicit too narrow a breadth of response, providing neither optimal protection nor protection on genetically diverse backgrounds. By contrast, to duplicate the protection induced by whole organism vaccination (Good, M.F. & Doolan, D.L. Immune effector mechanisms in malaria. *Curr. Opin. Immunol.* 11, 412-419 (1999)), a malaria vaccine targeting an unprecedented number of parasite-derived proteins through inclusion of their minimal CD8<sup>+</sup> and CD4<sup>+</sup> T cell epitopes in a multiepitope construct appears to be required. However, the antigens mediating whole organism induced protection are largely unknown.

[0004] Because of various factors, principally related to antigen abundance and immunodominance, not all possible antigens are recognized by natural immunity (Yewdell JW, Bennink JR. Immunodominance in major histocompatibility complex class



I-restricted T lymphocyte responses. Annu. Rev. Immunol. 17, 51-88. (1999)). Various approaches have been proposed for antigen identification, including expression cloning (Kawakami, Y. & Rosenberg, S. A. Immunobiology of human melanoma antigens MART-1 and gp100 and their use for immuno-gene therapy. Int. Rev. Immunol. 14, 173-192 (1997)), elution and mass spectrometry sequencing of naturally processed MHCbound peptides (Rotzschke, O. et al. Isolation and analysis of naturally processed viral peptides as recognized by cytotoxic T cells. Nature 348, 252-254 (1990); van Bleek, G. M. & Nathenson, S. G. Isolation of an endogenously processed immunodominant viral peptide from the class I H-2Kb molecule. Nature 348, 213-216 (1990); Hunt, D. F. et al. Peptides presented to the immune system by the murine class II major histocompatibility complex molecule I-Ad. Science 256, 1817-1820 (1992); Cox, A. L. et al. Identification of a peptide recognized by five melanoma-specific human cytotoxic T cell lines. Science 264, 716-719 (1994)), in vitro testing of pools of overlapping peptides (Kern, F. et al. Cytomegalovirus (CMV) Phosphoprotein 65 Makes a Large Contribution to Shaping the T Cell Repertoire in CMV-Exposed Individuals. J. Infect. Dis. 185, 1709-1716 (2002)), and reverse immunogenetics (Davenport, M. P. & Hill, A. V. Reverse immunogenetics: from HLA-disease associations to vaccine candidates. Mol. Med. Today 2, 38-45 (1996); Aidoo, M. et al. Identification of conserved antigenic components for a cytotoxic T lymphocyte-inducing vaccine against malaria. Lancet 345, 1003-1007 (1995)). However, these methods suffer from potential problems such as the repeated identification of the same (frequent/dominant) epitope, biases at the level of expansion of T cell populations, and use of clonal/oligoclonal T cells. They also tend to underestimate the complexity of responses, and are not able to analyze a large number of potential targets in the context of multiple HLA types. Finally, none of these approaches easily lends itself towards the daunting task of efficiently analyzing large amounts of genomic sequence data.

#### **Brief Summary**

[0005] The subject invention also provides novel Plasmodium falciparum antigens that are useful in therapeutic and diagnostic applications. In various aspects, the subject invention provides embodiments such as:

- A) isolated and/or purified polynucleotide sequences comprising:
- a polynucleotide sequence encoding a polypeptide sequence selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27;

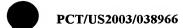


- b) a complementary polynucleotide sequence to a polynucleotide sequence encoding a polypeptide sequence selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27;
- c) a polynucleotide sequence having at least about 20% to 99.99% identity to a polynucleotide sequence of A(a) or A(b);
- d) a fragment of a polynucleotide sequence according to A(a) or A(b);
- e) a polynucleotide sequence encoding a polypeptide as set forth in Table 2, 3, 4, 5, or 6, or a polynucleotide sequence encoding a polypeptide selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27;
- f) a polynucleotide sequence encoding a variant of a polypeptide (e.g., a variant polypeptide) selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27;
- g) a polynucleotide sequence encoding a polypeptide fragment of a polypeptide selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27, wherein the fragment has substantially the same serologic reactivity as the native polypeptide and/or substantially the same T-cell reactivity as the native polypeptide or fragment;
- h) a polynucleotide sequence encoding a fragment of a variant polypeptide of a polypeptide selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27, wherein the fragment of the variant polypeptide has substantially the same serologic activity as the native polypeptide or substantially the same T-cell reactivity as the native polypeptide or fragment; or
- i) a polynucleotide sequence encoding a multi-epitope construct;

- B) primers or detection probes (e.g., fragments of the disclosed polynucleotide sequences) for hybridization with a target sequence or the amplicon generated from the target sequence comprising a sequence of at least 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100 consecutive nucleotides of the polynucleotide sequences set forth herein. Labeled probes or primers are labeled with a radioactive compound or with another type of label as set forth in embodiment C, below;
- C) isolated polynucleotides according to embodiments A or B further comprising a label; labels can include, and are not limited to 1) radioactive labels, 2) enzyme labels, 3) chemiluminescent labels, 4) fluorescent labels, 5) magnetic labels, or other suitable labels. Exemplary labels include, and are not limited to, <sup>32</sup>P, <sup>35</sup>S, <sup>3</sup>H, <sup>125</sup>I, biotin, acetylaminofluorene, digoxigenin, 5-bromo-deoxyuridine, or fluorescein;
- methods of detecting P. falciparum in biological samples D) comprising contacting a biological sample with isolated polynucleotides of embodiments A, B, or C. In this embodiment, P. falciparum cells, or cells comprising (infected) by P. falciparum are recovered, lysed, and DNA and/or RNA are extracted from the lysed cells. The extracted DNA or RNA is then tested using polynucleotides and/or probes set forth herein for the presence of P. falciparum. Typical assay formats utilizing nucleic acid hybridization includes, and are not limited to, 1) nuclear run-on assay, 2) slot blot assay, 3) northern blot assay (Alwine, et al. Proc. Natl. Acad. Sci. 74:5350), 4) magnetic particle separation, 5) nucleic Acid or DNA chips, 6) reverse Northern blot assay, 7) dot blot assay, 8) in situ hybridization, 9) RNase protection assay (Melton, et al. Nuc. Acids Res. 12:7035 and as described in the 1998 catalog of Ambion, Inc., Austin, Tex.), 10) ligase chain reaction, 11) polymerase chain reaction (PCR), 12) reverse transcriptase (RT)-PCR (Berchtold, et al. Nuc. Acids. Res. 17:453), 13) differential display RT-PCR (DDRT-PCR) or other suitable combinations of techniques and assays;



- E) analytical systems, such as DNA chips comprising polynucleotide sequences according to embodiments A, B, or C;
- modified polynucleotide sequences comprising polynucleotide F) sequences according to embodiments A or B;
- G) a polynucleotide sequence according to embodiments A, B, or F, further comprising regulatory sequences, such as promoters, enhancer elements, or termination sequences, that are operably linked to the polynucleotide sequences of embodiments A or B;
- a vector comprising a promoter operably linked to a nucleic acid H) sequence of the subject invention (e.g., as set forth in embodiments A, B, or F), optionally, one or more origins of replication, and, optionally, one or more selectable markers (e.g., an antibiotic resistance gene);
- host cells transformed by a vector according embodiment G or H. I) The host cell may be chosen from eukaryotic or prokaryotic systems, such as for example bacterial cells, (Gram negative or Gram positive), yeast cells, animal cells (such as Chinese hamster ovary (CHO) cells), plant cells, and/or insect cells using baculovirus vectors. In some embodiments, the host cells for expression of the polypeptides include, and are not limited to, those taught in U.S. Patent Nos. 6,319,691, 6,277,375, 5,643,570, or 5,565,335, each of which is incorporated by reference in its entirety, including all references cited within each respective patent.
- novel compositions comprising a pharmaceutically acceptable I) carrier and a polynucleotide according to embodiments A or B;
- methods of inducing an immune response or protective immune J) response in an individual comprising the administration of a composition comprising a polynucleotide according to embodiments A and/or B and a



pharmaceutically acceptable carrier in an amount sufficient to induce an immune response;

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- K) the method according to embodiment J, further comprising the administration of: 1) a viral vector comprising a polynucleotide according to embodiment A and/or B (or composition comprising the viral vector); and/or 2) a polypeptide antigen (or composition thereof) of the invention; in a preferred embodiment, the antigen is the polypeptide that is encoded by the polynucleotide administered as the polynucleotide vaccine. As a particularly preferred embodiment, the polypeptide antigen is administered as a booster subsequent to the initial administration of the polynucleotide vaccine. Exemplary viral vectors suitable for use in this embodiment include, but are not limited to, poxvirus such as vaccinia virus, avipox virus, fowlpox virus, a highly attenuated vaccinia virus (such as Ankara or MVA [Modified Vaccinia Ankara]), retrovirus, adenovirus, baculovirus and the like. In a preferred embodiment, the viral vector is Ankara or MVA;
- L) compositions comprising the polynucleotides of embodiments A, B, or F inserted into nucleic acid vaccine vectors (plasmids) or viral vectors and, optionally, a pharmaceutically acceptable carrier, e.g., saline;
  - M) one or more isolated polypeptides comprising:
  - a) a polypeptide encoded by a polynucleotide sequence according to embodiment A(a);
  - b) a variant polypeptide encoded by a polynucleotide sequence having at least about 20% to 99.99% identity to a polynucleotide according to embodiment A(a);
  - c) a fragment of a polypeptide or a variant polypeptide, wherein said fragment or variant has substantially the same serologic reactivity or substantially the same T-cell reactivity as the native polypeptide (e.g., those polypeptides set forth in SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27 and Tables 2, 3, 4, 5 or 6);



- d) a polypeptide sequence provided in Tables 2, 3, 4, 5 or 6 or selected from the group consisting of SEQ ID NO: NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27;
- e) a variant polypeptide having at least about 20% to 99.99% identity to a polypeptide provided in Tables 2, 3, 4, 5 or 6 or selected from the group consisting of SEQ ID NO: NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27;
  - f) a polypeptide (epitope) set forth in Table 2, 3, 4, 5 or 6; or
- g) a multi-epitope construct: 1) comprising at least one epitope set forth in Table 2, 3, 4, 5 or 6; 2) comprising a polypeptide selected from the group consisting of SEQ ID NO: NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27 and at least one epitope set forth in Tables 2, 3, 4, 5 and/or 6; or 3) comprising and at least one epitope set forth in Tables 2, 3, 4, 5 and/or 6 and one or more polypeptide selected from the group consisting of SEQ ID NO: NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27;
- N) a polypeptide epitope according to embodiment M(f), wherein the polypeptide epitope is a CTL-inducing peptides of about 13 residues or less in length, preferably between about 8 and about 11 residues (e.g., 8, 9, 10 or all residues), and more preferably 9 or 10 residues;
- O) a polypeptide epitope according to embodiment M(f), wherein the polypeptide epitope is a HTL-inducing peptide of less than about 50 residues, preferably, between about 6 and about 30 residues, more preferably, between about 12 and 25 residues (e.g., 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 residues), and most preferably, between about 15 and 20 residues (e.g., 15, 16, 17, 18, 19, or 20 residues);
- P) methods for eliciting an immune response in an individual comprising the administration of compositions comprising polypeptides according



to embodiment M or N to an individual in amounts sufficient to induce an immune response in the individual;

- Q) a composition comprising a pharmaceutically acceptable carrier and a polypeptide according to embodiment M or N, that can, optionally, contain an adjuvant;
- R) diagnostic assays based upon Western blot formats, or standard immunoassays known to the skilled artisan, comprising contacting a biological sample obtained from an individual with a polypeptide according to the embodiments M or N and detecting the formation of an antibody-antigen complex or detecting the stimulation of T-cells obtained from the individual (for example, as set forth in the Examples herein);
- S) a "multi-epitope construct" comprising: 1) polynucleotides that encode multiple polypeptide epitopes (of any length) that can bind to one or more molecules functioning in the immune system; or 2) polypeptides comprising multiple polypeptide epitopes that can bind to one or more molecules functioning in the immune system. Some embodiments provide for "multi-epitope constructs" that comprise a combination or series of different epitopes, optionally connected by "flanking" residues. "Multi-epitope constructs" can include the full length polypeptides from which the epitopes are obtained (e.g., the polypeptides of SEQ ID NOs: 1-27);
- T) a multi-epitope construct according to embodiment S, wherein the epitopes used in the formation of the multi-epitope construct are selected from those set forth in Table 2, Table, 3, Table 4, Table 5, and Table 6;
- U) a multi-epitope construct according to embodiments S or T that is of "high affinity" or "intermediate affinity";
- V) a multi-epitope construct according to embodiments S, T, or U that comprises five or more, ten or more, fifteen or more, twenty or more, or twenty-



five or more epitopes. Other embodiments provide multi-epitope constructs that comprise at least 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99 epitopes.

- W) a multi-epitope construct according to embodiments S, T, U, or V wherein: a) all of the epitopes in a multi-epitope construct are from one organism (e.g., the epitopes are obtained from P. falciparum); or b) or the multi-epitope construct includes epitopes present in two or more different organisms (e.g., some epitopes from P. falciparum and some epitopes from another organism). Additionally, the same epitope may be present in a multi-epitope construct at more than one location in the construct. In some embodiments, novel epitopes of the subject invention may be linked to known epitopes of an organism (e.g., P. falciparum or another organism).
- X) a multi-epitope construct according to embodiments S, T, U, V, or W, wherein the individual epitopes interact with an antigen binding site of an antibody molecule or fragment thereof, a class I HLA, a T-cell receptor, and/or a class II HLA molecule.
- Y) a multi-epitope construct according to embodiments S, T, U, V, W, or X, wherein the construct further comprises, optionally, 1 to 5 "flanking" or "linking" residues positioned next to one or more epitopes;
- Z) a multi-epitope construct according to embodiments S, T, U, V, W, X, or Y that has, optionally, been "optimized";
- AA) an isolated antibody or fragment thereof that specifically binds to a polypeptide as set forth in embodiments M or N;



BB) a viral vector comprising a polynucleotide according to embodiment A or B. Exemplary viral vectors suitable for use in this embodiment include, but are not limited to, poxvirus such as vaccinia virus, avipox virus, fowlpox virus, a highly attenuated vaccinia virus (such as Ankara or MVA [Modified Vaccinia Ankara]), retrovirus, adenovirus, baculovirus and the like. In a preferred embodiment, the viral vector is Ankara or MVA; and/or

a viral vector according to embodiment BB, wherein the viral CC) vector further comprises nucleic acids encoding immunostimulatory molecules such as IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-15, Il-16, Il-18, IL-23, IL-24, erythropoietin, G-CSF, M-CSF, platelet derived growth factor (PDGF), MSF, FLT-3 ligand, EGF, fibroblast growth factor (FGF; e.g., aFGF (FGF-1), bFGF (FGF-2), FGF-3, FGF-4, FGF-5, FGF-6, or FGF-7), insulinlike growth factors (e.g., IGF-1, IGF-2); vascular endothelial growth factor (VEGF); interferons (e.g., IFN-γ, IFN-α, IFN-β); leukemia inhibitory factor (LIF); ciliary neurotrophic factor (CNTF); oncostatin M; stem cell factor (SCF); transforming growth factors (e.g., TGF-\alpha, TGF-\beta1, TGF-\beta1), or chemokines (such as, but not limited to, BCA-1/BLC-1, BRAK/Kec, CXCL16, Exodus-2/SLC, Eotaxin-2/MPIF-2, Eotaxin-1, CXCR3. ENA-78/LIX, HCC-1. I-TAC. Fractalkine/Neur7otactin, GROalpha/MGSA, Lymphotactin/ATAC/SCM, MCP-1/MCAF, MCP-3, MCP-4, MDC/STCP-1, ABCD-1, MIP-1α, MIP-1β, MIP-2α/GROβ, MIP-3α/Exodus/LARC, MIP-3B/Exodus-3/ELC, MIP-4/PARC/DC-CK1, PF-4, RANTES, SDF1\alpha, TARC, or TECK).

#### Brief Description of Drawings and Tables

[0006] Table 1 presents a summary of immune reactivities of a panel of 27 novel antigens and four known antigens.

[0007] Tables 2-6 provide peptide epitopes of P. falciparum.

# Brief Description of Sequences

[0008] Sequence ID NOs: 1-27 are amino acid sequences of novel malaria antigens.

#### Detailed Disclosure

[0009] The subject invention provides isolated and/or purified novel P. falciparum polynucleotides and fragments of these novel polynucleotides. Thus, the present invention provides isolated and/or purified polynucleotide sequences comprising:

- a) a polynucleotide sequence encoding a polypeptide sequence selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27;
- b) a complementary polynucleotide sequence to a polynucleotide sequence encoding a polypeptide sequence selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27;
- c) a polynucleotide sequence having at least about 20% to 99.99% identity to a polynucleotide sequence of (a) or (b);
- d) a fragment of a polynucleotide sequence according to (a) or (b);
- e) a polynucleotide sequence encoding a polypeptide as set forth in Table 2, 3, 4, 5 or 6 or a polynucleotide sequence encoding a polypeptide selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27;
- f) a polynucleotide sequence encoding variant of a polypeptide (e.g., a variant polypeptide) selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27;
- g) a polynucleotide sequence encoding a polypeptide fragment of a polypeptide selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27, wherein the fragment has substantially the same serologic reactivity as the native polypeptide or

substantially the same T-cell reactivity as the native polypeptide or fragment;

- h) a polynucleotide sequence encoding a fragment of a variant polypeptide of a polypeptide selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27, wherein the fragment of the variant polypeptide has substantially the same serologic activity as the native polypeptide or substantially the same T-cell reactivity as the native polypeptide or fragment; or
- i) a polynucleotide sequence encoding a multi-epitope construct.

[0010] "Nucleotide sequence", "polynucleotide" or "nucleic acid" can be used interchangeably and are understood to mean, according to the present invention, either a double-stranded DNA, a single-stranded DNA or products of transcription of the said DNAs (e.g., RNA molecules). It should also be understood that the present invention does not relate to genomic polynucleotide sequences of P. falciparum in their natural environment or natural state. The nucleic acid, polynucleotide, or nucleotide sequences of the invention have been isolated, purified (or partially purified), by separation methods including, but not limited to, ion-exchange chromatography, molecular size exclusion chromatography, affinity chromatography, or by genetic engineering methods such as amplification, cloning, subcloning or chemical synthesis.

[0011] A homologous polynucleotide or polypeptide sequence, for the purposes of the present invention, encompasses a sequence having a percentage identity with the polynucleotide or polypeptide sequences, set forth herein, of between at least (or at least about) 20.00% to 99.99% (inclusive). The aforementioned range of percent identity is to be taken as including, and providing written description and support for, any fractional percentage, in intervals of 0.01%, between 20.00% and, up to, including 99.99%. These percentages are purely statistical and differences between two nucleic acid sequences can be distributed randomly and over the entire sequence length.



[0012] In various embodiments, homologous sequences can exhibit a percent identity of 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99 percent with the sequences of the instant invention. Typically, the percent identity is calculated with reference to the full length, native, and/or naturally occurring polypeptide or polynucleotide (e.g., those polypeptides set forth in SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27 or those set forth in SEQ ID NOs:28-81)). The terms "identical" or percent "identity", in the context of two or more polynucleotide or polypeptide sequences, refer to two or more sequences or subsequences that are the same or have a specified percentage of amino acid residues that are the same, when compared and aligned for maximum correspondence over a comparison window, as measured using a sequence comparison algorithm or by manual alignment and visual inspection. Preferably, such a substitution is made in accordance with analoging principles set forth, e.g., in co-pending U.S. Ser. No. 09/260,714 filed Mar. 1, 1999 and 09/226,775, filed January 6, 1999 and PCT application number PCT/US00/19774 each of which is hereby incorporated by reference in its entirety.

[0013] Both protein and nucleic acid sequence homologies may be evaluated using any of the variety of sequence comparison algorithms and programs known in the art. Such algorithms and programs include, but are by no means limited to, TBLASTN, BLASTP, FASTA, TFASTA, and CLUSTALW (Pearson and Lipman, 1988, Proc. Natl. Acad. Sci. USA 85(8):2444-2448; Altschul et al., 1990, J. Mol. Biol. 215(3):403-410; Thompson et al., 1994, Nucleic Acids Res. 22(2):4673-4680; Higgins et al., 1996, Methods Enzymol. 266:383-402; Altschul et al., 1990, J. Mol. Biol. 215(3):403-410; Altschul et al., 1993, Nature Genetics 3:266-272). Sequence comparisons are, typically, conducted using default parameters provided by the vendor or using those parameters set forth in the above-identified references, which are hereby incorporated by reference in their entireties.

[0014] A "complementary" polynucleotide sequence, as used herein, generally refers to a sequence arising from the hydrogen bonding between a particular purine and a particular pyrimidine in double-stranded nucleic acid molecules (DNA-DNA, DNA-



RNA, or RNA-RNA). The major specific pairings are guanine with cytosine and adenine A "complementary" polynucleotide sequence may also be with thymine or uracil. referred to as an "antisense" polynucleotide sequence or an "antisense" sequence.

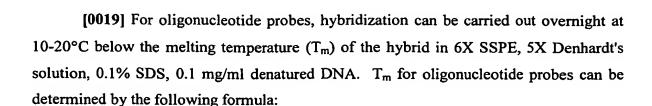
[0015] Sequence homology and sequence identity can also be determined by hybridization studies under high stringency, intermediate stringency, and/or low stringency. Various degrees of stringency of hybridization can be employed. The more severe the conditions, the greater the complementarity that is required for duplex formation. Severity of conditions can be controlled by temperature, probe concentration, probe length, ionic strength, time, and the like. Preferably, hybridization is conducted under low, intermediate, or high stringency conditions by techniques well known in the art, as described, for example, in Keller, G.H., M.M. Manak [1987] DNA Probes, Stockton Press, New York, NY, pp. 169-170.

[0016] For example, hybridization of immobilized DNA on Southern blots with <sup>32</sup>P-labeled gene-specific probes can be performed by standard methods (Maniatis et al. [1982] Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, New In general, hybridization and subsequent washes can be carried out under intermediate to high stringency conditions that allow for detection of target sequences with homology to the exemplified polynucleotide sequence. For double-stranded DNA gene probes, hybridization can be carried out overnight at 20-25° C below the melting temperature (T<sub>m</sub>) of the DNA hybrid in 6X SSPE, 5X Denhardt's solution, 0.1% SDS, 0.1 mg/ml denatured DNA. The melting temperature is described by the following formula (Beltz et al. [1983] Methods of Enzymology, R. Wu, L. Grossman and K. Moldave [eds.] Academic Press, New York 100:266-285).

[0017] Tm=81.5°C+16.6 Log[Na<sup>+</sup>]+0.41(%G+C)-0.61(%formamide)-600/length of duplex in base pairs.

# [0018] Washes are typically carried out as follows:

- (1) twice at room temperature for 15 minutes in 1X SSPE, 0.1% SDS (low stringency wash);
- (2) once at T<sub>m</sub> 20°C for 15 minutes in 0.2X SSPE, 0.1% SDS (intermediate stringency wash).



[0020] T<sub>m</sub> (°C)=2(number T/A base pairs)<sup>†</sup>4(number G/C base pairs) (Suggs et al. [1981] ICN-UCLA Symp. Dev. Biol. Using Purified Genes, D.D. Brown [ed.], Academic Press, New York, 23:683-693).

#### [0021] Washes can be carried out as follows:

- (1) twice at room temperature for 15 minutes 1X SSPE, 0.1% SDS (low stringency wash);
- 2) once at the hybridization temperature for 15 minutes in 1X SSPE, 0.1% SDS (intermediate stringency wash).

[0022] In general, salt and/or temperature can be altered to change stringency. With a labeled DNA fragment >70 or so bases in length, the following conditions can be used:

Low: 1 or 2X SSPE, room temperature

Low: 1 or 2X SSPE, 42°C

Intermediate: 0.2X or 1X SSPE, 65°C

High: 0.1X SSPE, 65°C.

[0023] By way of another non-limiting example, procedures using conditions of high stringency can also be performed as follows: Pre-hybridization of filters containing DNA is carried out for 8 h to overnight at 65°C in buffer composed of 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 μg/ml denatured salmon sperm DNA. Filters are hybridized for 48 h at 65°C, the preferred hybridization temperature, in pre-hybridization mixture containing 100 μg/ml denatured salmon sperm DNA and 5-20 x 10<sup>6</sup> cpm of <sup>32</sup>P-labeled probe. Alternatively, the hybridization step can be performed at 65°C in the presence of SSC buffer, 1X SSC

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corresponding to 0.15M NaCl and 0.05 M Na citrate. Subsequently, filter washes can be done at 37°C for 1 h in a solution containing 2X SSC, 0.01% PVP, 0.01% Ficoll, and 0.01% BSA, followed by a wash in 0.1X SSC at 50°C for 45 min. Alternatively, filter washes can be performed in a solution containing 2X SSC and 0.1% SDS, or 0.5X SSC and 0.1% SDS, or 0.1X SSC and 0.1% SDS at 68°C for 15 minute intervals. Following the wash steps, the hybridized probes are detectable by autoradiography. conditions of high stringency which may be used are well known in the art and as cited in Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, Second Edition, Cold Spring Harbor Press, N.Y., pp. 9.47-9.57; and Ausubel et al., 1989, Current Protocols in Molecular Biology, Green Publishing Associates and Wiley Interscience, N.Y. are incorporated herein in their entirety.

[0024] Another non-limiting example of procedures using conditions of intermediate stringency are as follows: Filters containing DNA are pre-hybridized, and then hybridized at a temperature of 60°C in the presence of a 5X SSC buffer and labeled probe. Subsequently, filters washes are performed in a solution containing 2X SSC at 50°C and the hybridized probes are detectable by autoradiography. Other conditions of intermediate stringency which may be used are well known in the art and as cited in Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, Second Edition, Cold Spring Harbor Press, N.Y., pp. 9.47-9.57; and Ausubel et al., 1989, Current Protocols in Molecular Biology, Green Publishing Associates and Wiley Interscience, N.Y. are incorporated herein in their entirety.

[0025] Duplex formation and stability depend on substantial complementarity between the two strands of a hybrid and, as noted above, a certain degree of mismatch can be tolerated. Therefore, the probe sequences of the subject invention include mutations (both single and multiple), deletions, insertions of the described sequences, and combinations thereof, wherein said mutations, insertions and deletions permit formation of stable hybrids with the target polynucleotide of interest. Mutations, insertions and deletions can be produced in a given polynucleotide sequence in many ways, and these methods are known to an ordinarily skilled artisan. Other methods may become known in the future.

[0026] It is also well known in the art that restriction enzymes can be used to obtain functional fragments of the subject DNA sequences. For example, Bal31

exonuclease can be conveniently used for time-controlled limited digestion of DNA (commonly referred to as "erase-a-base" procedures). See, for example, Maniatis et al. [1982] Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, New York; Wei et al. [1983] J. Biol. Chem. 258:13006-13512.

[0027] The present invention further comprises fragments of the polynucleotide sequences of the instant invention. Representative fragments of the polynucleotide sequences according to the invention will be understood to mean any nucleotide fragment having at least 8 successive nucleotides, preferably at least 12 successive nucleotides, and still more preferably at least 15 or at least 20 successive nucleotides of the sequence from which it is derived. The upper limit for such fragments is the total number of polynucleotides found in the full length sequence (or, in certain embodiments, of the full length open reading frame (ORF) identified herein).

[0028] In some embodiments, the subject invention includes those fragments capable of hybridizing under various conditions of stringency conditions (e.g., high or intermediate or low stringency) with a nucleotide sequence according to the invention; fragments that hybridize with a nucleotide sequence of the subject invention can be, optionally, labeled as set forth below.

[0029] Other embodiments provide for nucleic acid fragments corresponding to nucleotide sequences comprising full, or partial, open reading frames (ORF sequences). Also within the scope of the invention are those polynucleotide fragments encoding polypeptides reactive with antibodies found in the serum of individuals infected with *P. falciparum*. Fragments according to the subject invention can be obtained, for example, by specific amplification (e.g., PCR amplification), digestion with restriction enzymes, of nucleotide sequences according to the invention. Such methodologies are well-known in the art and are taught, for example, by Sambrook et al., 1989. Nucleic acid fragments according to the invention can also be obtained by chemical synthesis according to methods well known to persons skilled in the art.

[0030] The subject invention also provides nucleic acid based methods for the identification of the presence of an organism in a sample. In these varied embodiments, the invention provides for the detection of nucleic acids in a sample comprising contacting a sample with a nucleic acid (polynucleotide) of the subject invention (such as



an RNA, mRNA, DNA, cDNA, or other nucleic acid). In a preferred embodiment, the polynucleotide is a probe that is, optionally, labeled and used in the detection system. Many methods for detection of nucleic acids exist and any suitable method for detection is encompassed by the instant invention. Typical assay formats utilizing nucleic acid hybridization includes, and are not limited to, 1) nuclear run-on assay, 2) slot blot assay, 3) northern blot assay (Alwine, et al. Proc. Natl. Acad. Sci. 74:5350), 4) magnetic particle separation, 5) nucleic Acid or DNA chips, 6) reverse Northern blot assay, 7) dot blot assay, 8) in situ hybridization, 9) RNase protection assay (Melton, et al. Nuc. Acids Res. 12:7035 and as described in the 1998 catalog of Ambion, Inc., Austin, Tex.), 10) ligase chain reaction, 11) polymerase chain reaction (PCR), 12) reverse transcriptase (RT)-PCR (Berchtold, et al. Nuc. Acids. Res. 17:453), 13) differential display RT-PCR (DDRT-PCR) or other suitable combinations of techniques and assays. Labels suitable for use in these detection methodologies include, and are not limited to 1) radioactive labels, 2) enzyme labels, 3) chemiluminescent labels, 4) fluorescent labels, 5) magnetic labels, or other suitable labels, including those set forth below. These methodologies and labels are well known in the art and widely available to the skilled artisan. Likewise, methods of incorporating labels into the nucleic acids are also well known to the skilled artisan.

[0031] Thus, the subject invention also provides detection probes (e.g., fragments of the disclosed polynucleotide sequences) for hybridization with a target sequence or the amplicon generated from the target sequence. Such a detection probe will advantageously have as sequence a sequence of at least 8, 9, 10, 11, 12, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100 nucleotides. Labeled probes or primers are labeled with a radioactive compound or with another type of label as set forth above. Alternatively, non-labeled nucleotide sequences may be used directly as probes or primers; however, the sequences are generally labeled with a radioactive element (32P, 35S, 3H, 125I) or with a molecule such as biotin, acetylaminofluorene, digoxigenin, 5-bromo-deoxyuridine, or fluorescein to provide probes that can be used in numerous applications.

[0032] The polynucleotide sequences according to the invention may also be used in analytical systems, such as DNA chips. DNA chips and their uses are well known in the art and (see for example, U.S. Patent Nos. 5,561,071; 5,753,439; 6,214,545; Schena et al., BioEssays, 1996, 18:427-431; Bianchi et al., Clin. Diagn. Virol., 1997, 8:199-208;

each of which is hereby incorporated by reference in their entireties) and/or are provided by commercial vendors such as Affymetrix, Inc. (Santa Clara, CA). In addition, the nucleic acid sequences of the subject invention can be used as molecular weight markers in nucleic acid analysis procedures.

[0033] The subject invention also provides for modified nucleotide sequences. Modified nucleic acid sequences will be understood to mean any nucleotide sequence that has been modified, according to techniques well known to persons skilled in the art, and exhibiting modifications in relation to the native, naturally occurring nucleotide sequences. One non-limiting example of a "modified" nucleotide sequences includes mutations in regulatory and/or promoter sequences of a polynucleotide sequence that result in a modification of the level of expression of the polypeptide. A "modified" nucleotide sequence will also be understood to mean any nucleotide sequence encoding a "modified" polypeptide as defined below.

[0034] Another aspect of the invention provides vectors for the cloning and/or the expression of a polynucleotide sequence taught herein. Vectors of this invention, including vaccine vectors, can also comprise elements necessary to allow the expression and/or the secretion of the said nucleotide sequences in a given host cell. The vector can contain a promoter, signals for initiation and for termination of translation, as well as appropriate regions for regulation of transcription. In certain embodiments, the vectors can be stably maintained in the host cell and can, optionally, contain signal sequences directing the secretion of translated protein. These different elements are chosen according to the host cell used. Vectors can integrate into the host genome or, optionally, be autonomously-replicating vectors.

[0035] The subject invention also provides for the expression of a polypeptide, peptide, derivative, or variant encoded by a polynucleotide sequence disclosed herein comprising the culture of an organism transformed with a polynucleotide of the subject invention under conditions that allow for the expression of the polypeptide, peptide, derivative, or analog and, optionally, recovering the expressed polypeptide, peptide, derivative, or analog.

[0036] The disclosed polynucleotide sequences can also be regulated by a second nucleic acid sequence so that the protein or peptide is expressed in a host transformed

with the recombinant DNA molecule. For example, expression of a protein or peptide may be controlled by any promoter/enhancer element known in the art. Promoters which may be used to control expression include, but are not limited to, the CMV-IE promoter, the SV40 early promoter region (Bernoist and Chambon, 1981, Nature 290:304-310), the promoter contained in the 3' long terminal repeat of Rous sarcoma virus (Yamamoto, et al., 1980, Cell 22:787-797), the herpes simplex thymidine kinase promoter (Wagner et al., 1981, Proc. Natl. Acad. Sci. U.S.A. 78:1441-1445), the regulatory sequences of the metallothionein gene (Brinster et al., 1982, Nature 296:39-42); prokaryotic vectors containing promoters such as the β-lactamase promoter (Villa-Kamaroff, et al., 1978, Proc. Natl. Acad. Sci. U.S.A. 75:3727-3731), or the tac promoter (DeBoer, et al., 1983, Proc. Natl. Acad. Sci. U.S.A. 80:21-25); see also "Useful proteins from recombinant bacteria" in Scientific American, 1980, 242:74-94; plant expression vectors comprising the nopaline synthetase promoter region (Herrera-Estrella et al., 1983, Nature 303:209-213) or the cauliflower mosaic virus 35S RNA promoter (Gardner, et al., 1981, Nucl. Acids Res. 9:2871), and the promoter of the photosynthetic enzyme ribulose biphosphate carboxylase (Herrera-Estrella et al., 1984, Nature 310:115-120); promoter elements from

[0037] The vectors according to the invention are, for example, vectors of plasmid or viral origin. In a specific embodiment, a vector is used that comprises a promoter operably linked to a protein or peptide-encoding nucleic acid sequence contained within the disclosed polynucleotide sequences, one or more origins of replication, and, optionally, one or more selectable markers (e.g., an antibiotic resistance gene). Expression vectors comprise regulatory sequences that control gene expression, including gene expression in a desired host cell. Exemplary vectors for the expression of the polypeptides of the invention include the pET-type plasmid vectors (Promega) or pBAD plasmid vectors (Invitrogen) or those provided in the examples below. Furthermore, the vectors according to the invention are useful for transforming host cells so as to clone or express the polynucleotide sequences of the invention.

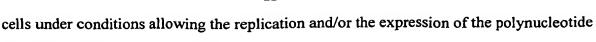
yeast or fungi such as the Gal 4 promoter, the ADC (alcohol dehydrogenase) promoter,

PGK (phosphoglycerol kinase) promoter, and/or the alkaline phosphatase promoter.

[0038] The invention also encompasses the host cells transformed by a vector according to the invention. These cells may be obtained by introducing into host cells a nucleotide sequence inserted into a vector as defined above, and then culturing the said

sequences of the subject invention.

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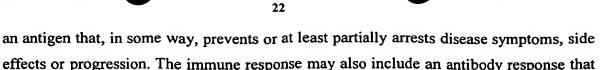


[0039] The host cell may be chosen from eukaryotic or prokaryotic systems, such as for example bacterial cells, (Gram negative or Gram positive), yeast cells (for example, Saccharomyces cereviseae or Pichia pastoris), animal cells (such as Chinese hamster ovary (CHO) cells), plant cells, and/or insect cells using baculovirus vectors. In some embodiments, the host cells for expression of the polypeptides include, and are not limited to, those taught in U.S. Patent Nos. 6,319,691, 6,277,375, 5,643,570, or 5,565,335, each of which is incorporated by reference in its entirety, including all references cited within each respective patent.

[0040] Furthermore, a host cell strain may be chosen which modulates the expression of the inserted sequences, or modifies and processes the gene product in the specific fashion desired. Expression from certain promoters can be elevated in the presence of certain inducers; thus, expression of the genetically engineered polypeptide may be controlled. Furthermore, different host cells have characteristic and specific mechanisms for the translational and post-translational processing and modification (e.g., glycosylation, phosphorylation) of proteins. Appropriate cell lines or host systems can be chosen to ensure the desired modification and processing of the foreign protein expressed. For example, expression in a bacterial system can be used to produce an unglycosylated core protein product. Expression in yeast will produce a glycosylated product. Expression in mammalian cells can be used to ensure "native" glycosylation of a heterologous protein. Furthermore, different vector/host expression systems may effect processing reactions to different extents.

[0041] The subject invention also concerns novel compositions that can be employed to elicit an immune response or a protective immune response. In this aspect of the invention, an amount of a composition comprising recombinant DNA or mRNA encoding an polynucleotide of the subject invention sufficient to elicit an immune response or protective immune response is administered to an individual. Signal sequences may be deleted from the nucleic acid encoding an antigen of interest and the individual may be monitored for the induction of an immune response according to methods known in the art. A "protective immune response" or "therapeutic immune response" refers to a CTL (or CD8<sup>+</sup> T cell) and/or an HTL (or CD4<sup>+</sup> T cell) response to

has been facilitated by the stimulation of helper T cells.



[0042] In another embodiment, the subject invention further comprises the administration of polynucleotide vaccines in conjunction with a polypeptide antigen, or composition thereof, of the invention. In a preferred embodiment, the antigen is the polypeptide that is encoded by the polynucleotide administered as the polynucleotide vaccine. As a particularly preferred embodiment, the polypeptide antigen is administered as a booster subsequent to the initial administration of the polynucleotide vaccine.

[0043] A further embodiment of the subject invention provides for the induction of an immune response to the novel Plasmodium falciparum antigens disclosed herein (see, for example, the antigens and peptides set forth in the Tables and Sequence Listing attached hereto) using a "prime-boost" vaccination regimen known to those skilled in the art. In this aspect of the invention, a DNA vaccine is administered to an individual in an amount sufficient to "prime" the immune response of the individual, provided that the DNA vaccine comprises nucleic acids encoding the antigens, multi-epitope constructs, and/or peptide antigens set forth herein. The immune response of the individual is then "boosted" via the administration of: 1) one or a combination of: a peptide, polypeptide, and/or full length polypeptide antigen (e.g., SEQ ID NOs: 1-27) of the subject invention (optionally in conjunction with a immunostimulatory molecule and/or an adjuvant); or 2) a viral vector that contains nucleic acid encoding one, or more, of the same or, optionally, different, antigens, multi-epitope constructs, and/or peptide antigens set forth in the Tables or Sequence Listing of the subject application. In some alternative embodiments of the invention, a gene encoding an immunostimulatory molecule may be incorporated into the viral vector used to "boost the immune response of the individual. Exemplary immunostimulatory molecules include, and are not limited to, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-15, Il-16, Il-18, IL-23, IL-24, erythropoietin, G-CSF, M-CSF, platelet derived growth factor (PDGF), MSF, FLT-3 ligand, EGF, fibroblast growth factor (FGF; e.g., aFGF (FGF-1), bFGF (FGF-2), FGF-3, FGF-4, FGF-5, FGF-6, or FGF-7), insulin-like growth factors (e.g., IGF-1, IGF-2); vascular endothelial growth factor (VEGF); interferons (e.g., IFN-γ, IFN-α, IFN-β); leukemia inhibitory factor (LIF); ciliary neurotrophic factor (CNTF); oncostatin M; stem cell factor



(SCF); transforming growth factors (e.g., TGF-α, TGF-β1, TGF-β1, TGF-β1), or chemokines (such as, but not limited to, BCA-1/BLC-1, BRAK/Kec, CXCL16, CXCR3, ENA-78/LIX, Eotaxin-1, Eotaxin-2/MPIF-2, Exodus-2/SLC, Fractalkine/Neurotactin, GROalpha/MGSA, HCC-1, I-TAC, Lymphotactin/ATAC/SCM, MCP-1/MCAF, MCP-3, MDC/STCP-1, ABCD-1, MIP-1 $\alpha$ , MIP-1 $\beta$ , MIP-2 $\alpha$ /GRO $\beta$ , 3α/Exodus/LARC, MIP-3β/Exodus-3/ELC, MIP-4/PARC/DC-CK1, PF-4, RANTES, SDF1a, TARC, or TECK). Genes encoding these immunostimulatory molecules are known to those skilled in the art and coding sequences may be obtained from a variety of sources, including various patents databases, publicly available databases (such as the nucleic acid and protein databases found at the National Library of Medicine or the European Molecular Biology Laboratory), the scientific literature, or scientific literature cited in catalogs produced by companies such as Genzyme, Inc., R&D Systems, Inc, or InvivoGen, Inc. [see, for example, the 1995 Cytokine Research Products catalog, Genzyme Diagnostics, Genzyme Corporation, Cambridge MA; 2002 or 1995 Catalog of R&D Systems, Inc (Minneapolis, MN); or 2002 Catalog of InvivoGen, Inc (San Diego, CA) each of which is incorporated by reference in its entirety, including all references cited therein].

[0044] Methods of introducing DNA vaccines into individuals are well-known to the skilled artisan. For example, DNA can be injected into skeletal muscle or other somatic tissues (e.g., intramuscular injection). Cationic liposomes or biolistic devices, such as a gene gun, can be used to deliver DNA vaccines. Alternatively, iontophoresis and other means for transdermal transmission can be used for the introduction of DNA vaccines into an individual.

[0045] Viral vectors for use in the subject invention can have a portion of the viral genome deleted to introduce new genes without destroying infectivity of the virus. The viral vector of the present invention is, typically, a non-pathogenic virus. At the option of the practitioner, the viral vector can be selected so as to infect a specific cell type, such as professional antigen presenting cells (e.g., macrophage or dendritic cells). Alternatively, a viral vector can be selected that is able to infect any cell in the individual. Exemplary viral vectors suitable for use in the present invention include, but are not limited to poxvirus such as vaccinia virus, avipox virus, fowlpox virus, a highly attenuated vaccinia

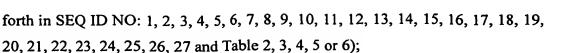
virus (such as Ankara or MVA [Modified Vaccinia Ankara]), retrovirus, adenovirus, baculovirus and the like. In a preferred embodiment, the viral vector is Ankara or MVA.

[0046] General strategies for construction of vaccinia virus expression vectors are known in the art (see, for example, Smith and Moss Bio Techniques Nov/Dec, 306-312, 1984; U.S. Patent No. 4,738,846 (hereby incorporated by reference in its entirety). Sutter and Moss (Proc. Nat'l. Acad. Sci U.S.A. 89:10847-10851, 1992) and Sutter et al. (Vaccine, 12(11):1032-40, 1994) disclose the construction and use as a vector, a non-replicating recombinant Ankara virus (MVA) which can be used as a viral vector in the present invention. Other versions of the Modified Vaccinia Ankara strain can also be used in the practice of the subject invention (such as the MVA-BN strain produced by Bavarian Nordic S/A (Copenhagen, Denmark).

[0047] Compositions comprising the subject polynucleotides can include appropriate nucleic acid vaccine vectors (plasmids), which are commercially available (e.g., Vical, San Diego, CA) or other nucleic acid vectors (plasmids), which are also commercially available (e.g., Valenti, Burlingame, CA). Alternatively, compositions comprising viral vectors and polynucleotides according to the subject invention are provided by the subject invention. In addition, the compositions can include a pharmaceutically acceptable carrier, e.g., saline. The pharmaceutically acceptable carriers are well known in the art and also are commercially available. For example, such acceptable carriers are described in E.W. Martin's Remington's Pharmaceutical Science, Mack Publishing Company, Easton, PA.

[0048] The subject invention also provides one or more isolated polypeptides comprising:

- a) a polypeptide encoded by a polynucleotide sequence according to embodiment A(a) (set forth above);
- b) a variant polypeptide encoded by a polynucleotide sequence having at least about 20% to 99.99% identity to a polynucleotide according to embodiment A(a) (as set forth above);
- c) a fragment of a polypeptide or a variant polypeptide, wherein said fragment or variant has substantially the same serologic reactivity or substantially the same T-cell reactivity as the native polypeptide (e.g., those polypeptides set



- d) a polypeptide sequence provided in Table 2, 3, 4, 5 or 6 or selected from the group consisting of SEQ ID NO: NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27;
- e) a variant polypeptide having at least about 20% to 99.99% identity to a polypeptide provided in Table 2, 3, 4, 5 or 6 or selected from the group consisting of SEQ ID NO: NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27;
  - f) a polypeptide (epitope) set forth in Table 2, 3, 4, 5 or 6; or
- g) a multi-epitope construct: 1) comprising at least one epitope set forth in Table 2, 3, 4, 5 or 6; 2) comprising a polypeptide selected from the group consisting of SEQ ID NO: NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27 and at least one epitope set forth in Tables 2, 3, 4, 5 or 6; or 3) comprising and at least one epitope set forth in Tables 2, 3, 4, 5 or 6 and one or more polypeptide selected from the group consisting of SEQ ID NO: NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27.

[0049] The term "peptide" may be used interchangeably with "oligopeptide" or "polypeptide" or "epitope" in the present specification to designate a series of residues, typically L-amino acids, connected one to the other, typically by peptide bonds between the α-amino and carboxyl groups of adjacent amino acids. The preferred CTL (or CD8<sup>+</sup> T cell)-inducing peptides of the invention are 13 residues or less in length and usually consist of between about 8 and about 11 residues (e.g., 8, 9, 10 or 11 residues), preferably 9 or 10 residues. The preferred HTL (or CD4<sup>+</sup> T cell)-inducing peptides are less than about 50 residues in length and usually consist of between about 6 and about 30 residues, more usually between about 12 and 25 (e.g., 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 or 25), and often between about 15 and 20 residues (e.g., 15, 16, 17, 18, 19 or 20).

[0050] According to the subject invention, a "fragment" is a polypeptide of at least 3 consecutive, preferably 4 consecutive, and even more preferably 5 consecutive amino acids. In some embodiments, the polypeptide fragments are reactive with antibodies found in the serum of an individual. In other embodiments, a fragment is

an "epitope" as described *supra*. In the context of the instant invention, the terms polypeptide, peptide and protein can be used interchangeably; however, it should be understood that the invention does not relate to the polypeptides in natural form, that is to say that they are not in their natural environment but that the polypeptides may have been isolated or obtained by purification from natural sources, obtained from host cells prepared by genetic manipulation (*e.g.*, the polypeptides, or fragments thereof, are recombinantly produced by host cells, or by chemical synthesis). Polypeptides according to the instant invention may also contain non-natural amino acids, as will be described below.

[0051] A "variant" or "modified" polypeptide (or polypeptide variant) is to be understood to designate polypeptides exhibiting, in relation to the natural polypeptide, certain modifications. These modifications can include a deletion, addition, or substitution of at least one amino acid, a truncation, an extension, a chimeric fusion, a mutation, or polypeptides exhibiting post-translational modifications. Among the homologous polypeptides, those whose amino acid sequences exhibit between at least (or at least about) 20.00% to 99.99% (inclusive) identity to the full length, native, or naturally occurring polypeptide are another aspect of the invention. The aforementioned range of percent identity is to be taken as including, and providing written description and support for, any fractional percentage, in intervals of 0.01%, between 20.00% and, up to, including 99.99%. These percentages are purely statistical and differences between two polypeptide sequences can be distributed randomly and over the entire sequence length.

[0052] Variant peptides (epitopes) can also be created by altering the presence or absence of particular residues in these primary anchor positions. Such analogs are used to modulate the binding affinity of a peptide comprising a particular motif or supermotif. The term "motif" refers to the pattern of residues in a peptide of defined length, usually a peptide of from about 8 to about 13 amino acids for a class I HLA motif (e.g., 8, 9, 10, 11, 12 or 13 aa) and from about 6 to about 25 amino acids for a class II HLA motif (e.g., 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 or 25 amino acids), which is recognized by a particular HLA molecule. Peptide motifs are typically different for each protein encoded by each human HLA allele and differ in the pattern of the primary and secondary anchor residues. Optionally, variant peptides or polypeptides can also comprise one or more heterologous polypeptide sequences (e.g., tags that facilitate

27 purification of the polypeptides of the invention (see, for example, U.S. Patent No. 6,342,362, hereby incorporated by reference in its entirety; Altendorf et al. [1999-WWW, 2000] "Structure and Function of the Fo Complex of the ATP Synthase from Escherichia Coli," J. of Experimental Biology 203:19-28, The Co. of Biologists, Ltd., G.B.; Baneyx [1999] "Recombinant Protein Expression in Escherichia coli," Biotechnology 10:411-21, Elsevier Science Ltd.; Eihauer et al. [2001] "The FLAG™ Peptide, a Versatile Fusion Tag for the Purification of Recombinant Proteins," J. Biochem Biophys Methods 49:455-65; Jones et al. [1995] J. Chromatography 707:3-22; Jones et al. [1995] "Current Trends in Molecular Recognition and Bioseparation," J. of Chromatography A. 707:3-22, Elsevier Science B.V.; Margolin [2000] "Green Fluorescent Protein as a Reporter for Macromolecular Localization in Bacterial Cells," Methods 20:62-72, Academic Press; Puig et al. [2001] "The Tandem Affinity Purification (TAP) Method: A General Procedure of Protein Complex Purification," Methods 24:218-29, Academic Press; Sassenfeld [1990] "Engineering Proteins for Purification," TibTech 8:88-93; Sheibani [1999] "Prokaryotic Gene Fusion Expression Systems and Their Use in Structural and Functional Studies of Proteins," Prep. Biochem. & Biotechnol. 29(1):77-90, Marcel Dekker, Inc.; Skerra et al. [1999] "Applications of a Peptide Ligand for Streptavidin: the Strep-tag", Biomolecular Engineering 16:79-86, Elsevier Science, B.V.; Smith [1998] "Cookbook for Eukaryotic Protein Expression: Yeast, Insect, and Plant Expression Systems," The Scientist 12(22):20; Smyth et al. [2000] "Eukaryotic Expression and Purification of Recombinant Extracellular Matrix Proteins Carrying the Strep II Tag", Methods in Molecular Biology, 139:49-57; Unger [1997] "Show Me the Money: Prokaryotic Expression Vectors and Purification Systems," The Scientist 11(17):20, each of which is hereby incorporated by reference in their entireties), or commercially available tags from vendors such as such as STRATAGENE (La Jolla, CA), NOVAGEN (Madison, WI), QIAGEN, Inc., (Valencia,

[0053] Variant polypeptides can, alternatively, have 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99 percent identity with the polypeptide sequences of the instant invention. In a preferred embodiment, a variant or modified polypeptide exhibits approximately 85%, 86%, 87%,

CA), or InVitrogen (San Diego, CA).



88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to a natural polypeptic of the invention. Typically, the percent identity is calculated with reference to the full length, native, and/or naturally occurring polypeptide (e.g., those polypeptides set forth in SEO ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, or 27).

[0054] The nomenclature used to describe peptide compounds follows the conventional practice wherein the amino group is presented to the left (the N-terminus) and the carboxyl group to the right (the C-terminus) of each amino acid residue. When amino acid residue positions are referred to in an epitope, they are numbered in an amino to carboxyl direction with position one being the position closest to the amino terminal end of the epitope, or the peptide or protein of which it may be a part. In the formulae representing selected specific embodiments of the present invention, the amino- and carboxyl-terminal groups, although not specifically shown, are in the form they would assume at physiologic pH values, unless otherwise specified. In the amino acid structure formulae, each residue is generally represented by standard three-letter or single-letter designations (e.g., as set forth infra). By way of example, amino acid substitutions can be carried out without resulting in a substantial modification of the biological activity of the corresponding modified polypeptides; for example, the replacement of leucine with valine or isoleucine, of aspartic acid with glutamic acid, of glutamine with asparagine, of arginine with lysine, and the like, the reverse substitutions can be performed without substantial modification of the biological activity of the polypeptides.

[0055] The L-form of an amino acid residue is represented by a capital single letter or a capital first letter of a three-letter symbol, and the D-form, for those amino acids having D-forms, is represented by a lower case single letter or a lower case three letter symbol. Glycine has no asymmetric carbon atom and is simply referred to as "Gly" or G. Symbols for the amino acids are as follows: (Single Letter Symbol; Three Letter Symbol Amino Acid) A; Ala; Alanine: C; Cys; Cysteine: D; Asp; Aspartic Acid: E; Glu; Glutamic Acid: F; Phe; Phenylalanine: G; Gly; Glycine: H; His; Histidine: I; Ile; Isoleucine: K; Lys; Lysine: L; Leu; Leucine: M; Met; Methionine: N; Asn; Asparagine: P; Pro; Proline: Q; Gln; Glutamine: R; Arg; Arginine: S; Ser; Serine: T; Thr; Threonine: V; Val; Valine: W; Trp; Tryptophan: Y; Tyr; Tyrosine.

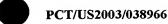


[0056] Amino acid "chemical characteristics" are defined as: Aromatic (F, W, Y); Aliphatic-hydrophobic (L, I, V, M); Small polar (S, T, C); Large polar (Q, N); Acidic (D, E); Basic (R, H, K); Non-polar: Proline; Alanine; and Glycine.

[0057] In order to extend the life of the polypeptides according to the invention, it may be advantageous to use non-natural amino acids, for example in the D-form, or alternatively amino acid analogs, for example sulfur-containing forms of amino acids in the production of "variant polypeptides". Alternative means for increasing the life of polypeptides can also be used in the practice of the instant invention. For example, polypeptides of the invention, and fragments thereof, can be recombinantly modified to include elements that increase the plasma, or serum half-life of the polypeptides of the invention. These elements include, and are not limited to, antibody constant regions (see for example, U.S. Patent No. 5,565,335, hereby incorporated by reference in its entirety, including all references cited therein), or other elements such as those disclosed in U.S. Patent Nos. 6,319,691, 6,277,375, or 5,643,570, each of which is incorporated by reference in its entirety, including all references cited within each respective patent. Alternatively, the polynucleotides and genes of the instant invention can be recombinantly fused to elements, well known to the skilled artisan, that are useful in the preparation of immunogenic constructs for the purposes of vaccine formulation.

[0058] The subject invention also provides biologically active fragments (epitopes) of a polypeptide according to the invention and includes those peptides capable of eliciting an immune response directed against *P. falciparum*, said immune response providing components (B-cells, antibodies, and/or or components of the cellular immune response (e.g., helper, cytotoxic, and/or suppressor T-cells)) reactive with the biologically active fragment of a polypeptide; the intact, full length, unmodified polypeptide disclosed herein; or both the biologically active fragment of a polypeptide and the intact, full length, unmodified polypeptides disclosed herein.

[0059] Fragments, as described herein, can be obtained by cleaving the polypeptides of the invention with a proteolytic enzyme (such as trypsin, chymotrypsin, or collagenase) or with a chemical reagent, such as cyanogen bromide (CNBr). Alternatively, polypeptide fragments can be generated in a highly acidic environment, for example at pH 2.5. Such polypeptide fragments may be equally well prepared by chemical synthesis or using hosts transformed with an expression vector according to the



invention. The transformed host cells contain a nucleic acid, allowing the expression of these fragments, under the control of appropriate elements for regulation and/or expression of the polypeptide fragments.

[0060] In one embodiment, the subject invention provides methods for eliciting an immune response in an individual comprising the administration of compositions comprising polypeptides according to the subject invention to an individual in amounts sufficient to induce an immune response in the individual. In some embodiments, a "protective" or "therapeutic immune response" is induced in the individual. "protective immune response" or "therapeutic immune response" refers to a CTL (or CD8<sup>+</sup> T cell) and/or an HTL (or CD4<sup>+</sup> T cell), and/or an antibody response to an antigen derived from an infectious agent or a tumor antigen, which in some way prevents or at least partially arrests disease symptoms, side effects or progression. The protective immune response may also include an antibody response that has been facilitated by the stimulation of helper T cells (or CD4<sup>+</sup> T cells). Additional methods of inducing an immune response in an individual are taught in U.S. Patent No. 6,419,931, hereby incorporated by reference in its entirety. The term CTL can be used interchangeably with CD8<sup>+</sup> T-cell(s) and the term HTL can be used interchangeably with CD4<sup>+</sup> T-cell(s) throughout the subject application.

[0061] The term "individual" includes mammals which include, and are not limited to, apes, chimpanzees, orangutans, humans, monkeys or domesticated animals (pets) such as dogs, cats, guinea pigs, hamsters, Vietnamese pot-bellied pigs, rabbits, ferrets, cows, horses, goats and sheep. In a preferred embodiment, the methods of inducing an immune response contemplated herein are practiced on humans.

[0062] Another embodiment of the subject invention provides methods of inducing an immune response in an individual comprising the administration of a composition comprising polypeptides encoded by the polynucleotides of the subject invention in amounts sufficient to induce an immune response. In some embodiments of the invention, the immune response provides protective immunity. The composition administered to the individual may, optionally, contain an adjuvant and may be delivered in any manner known in the art for the delivery of immunogen to a subject. Compositions may also be formulated in any carriers, including for example, pharmaceutically acceptable carriers such as those described in E.W. Martin's



Remington's Pharmaceutical Science, Mack Publishing Company, Easton, PA. In a preferred embodiment, compositions may be formulated in incomplete Freund's adjuvant.

[0063] In various embodiments, the subject invention provides for diagnostic assays based upon Western blot formats or standard immunoassays known to the skilled artisan. For example, antibody-based assays such as enzyme linked immunosorbent assays (ELISAs), radioimmunoassays (RIAs), lateral flow assays, immunochromatographic strip assays, automated flow assays, and assays utilizing antibody-containing biosensors may be employed for the detection of the polypeptides, and fragments thereof, provided by the subject invention. The assays and methods for conducting the assays are well-known in the art and the methods may test biological samples qualitatively (presence or absence of polypeptide) or quantitatively (comparison of a sample against a standard curve prepared using a polypeptide of the subject invention) for the presence of one or more polypeptide of the subject invention. Thus, the subject invention provides a method of detecting a P. falciparum polypeptide, or fragment thereof, comprising contacting a sample with an antibody that specifically binds to a polypeptide, or fragment thereof, comprising SEQ ID NOs: 1-26, or 27 and detecting the presence of an antibody-antigen complex.

[0064] The antibody-based assays can be considered to be of four types: direct binding assays, sandwich assays, competition assays, and displacement assays. In a direct binding assay, either the antibody or antigen is labeled, and there is a means of measuring the number of complexes formed. In a sandwich assay, the formation of a complex of at least three components (e.g., antibody-antigen-antibody) is measured. In a competition assay, labeled antigen and unlabelled antigen compete for binding to the antibody, and either the bound or the free component is measured. In a displacement assay, the labeled antigen is pre-bound to the antibody, and a change in signal is measured as the unlabelled antigen displaces the bound, labeled antigen from the receptor.

[0065] Lateral flow assays can be conducted according to the teachings of U.S. Patent No. 5,712,170 and the references cited therein. U.S. Patent No. 5,712,170 and the references cited therein are hereby incorporated by reference in their entireties. Displacement assays and flow immunosensors useful for carrying out displacement assays are described in: (1) Kusterbeck et al., "Antibody-Based Biosensor for Continuous Monitoring", in Biosensor Technology, R. P. Buck et al., eds., Marcel Dekker, N.Y. pp.

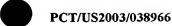


345-350 (1990); Kusterbeck et al., "A Continuous Flow Immunoassay for Rapid and Sensitive Detection of Small Molecules", Journal of Immunological Methods, vol. 135, pp. 191-197 (1990); Ligler et al., "Drug Detection Using the Flow Immunosensor", in Biosensor Design and Application, J. Findley et al., eds., American Chemical Society Press, pp. 73-80 (1992); and Ogert et al., "Detection of Cocaine Using the Flow Immunosensor", Analytical Letters, vol. 25, pp. 1999-2019 (1992), all of which are incorporated herein by reference in their entireties. Displacement assays and flow immunosensors are also described in U.S. Patent No. 5,183,740, which is also incorporated herein by reference in its entirety. The displacement immunoassay, unlike most of the competitive immunoassays used to detect small molecules, can generate a positive signal with increasing antigen concentration. One aspect of the invention allows for the exclusion of Western blots as a diagnostic assay, particularly where the Western blot is a screen of whole cell lysates of P. falciparum, or related organisms, against immune serum of infected individuals. In another aspect of the invention, peptide, or polypeptide, based diagnostic assays utilize P. falciparum peptides or polypeptides that have been produce either by chemical peptide synthesis or by recombinant methodologies that utilize non-plasmodium host cells for the production of peptides or polypeptides.

[0066] Another aspect of the invention provides for the use of peptides, polypeptides, and multi-epitope constructs in assays such as those taught in U.S. Patent No. 5,635,363, which is hereby incorporated by reference in its entirety. peptides, polypeptides, and multi-epitope constructs of the subject invention can be used to form stable multimeric complexes that comprise prepared major histocompatibility complex (MHC) protein subunits having a substantially homogeneous bound peptide population. The multimeric MHC-antigen complex forms a stable structure with T cells recognizing the complex through their antigen receptor, thereby allowing for the labeling, identification and separation of specific T cells. The multimeric binding complex has the formula  $(\alpha-\beta-P)_n$ , where  $n \ge 2$ , usually  $n \ge 4$ , and usually  $n \le 10$ ;  $\alpha$  is an  $\alpha$  chain of a class I or class II MHC protein.  $\beta$  is a  $\beta$  chain, (the  $\beta$  chain of a class II MHC protein or  $\beta_2$ microglobulin for a MHC class I protein; and P is a peptide antigen. The multimeric complex stably binds through non-covalent interactions to a T cell receptor having the appropriate antigenic specificity. The MHC proteins may be from any individual. Of particular interest are the human HLA proteins. Included in the HLA proteins are the

class II subunits HLA-DPα, HLA-DPβ, HLA-DQα, HLA-DQβ, HLA-DRα and HLA-DRβ, and the class I proteins HLA-A, HLA-B, HLA-C, and β<sub>2</sub> -microglobulin. preferred embodiment, the MHC protein subunits are a soluble form of the normally membrane-bound protein. The soluble form is derived from the native form by deletion of the transmembrane domain. Conveniently, the protein is truncated, removing both the cytoplasmic and transmembrane domains. The protein may be truncated by proteolytic cleavage, or by expressing a genetically engineered truncated form. For class I proteins, the soluble form will include the  $\alpha 1$ ,  $\alpha 2$  and  $\alpha 3$  domain. Not more than about 10, usually not more than about 5, preferably none of the amino acids of the transmembrane domain will be included. The deletion may extend as much as about 10 amino acids into the  $\alpha$ 3 domain, preferably none of the amino acids of the a domain will be deleted. The deletion will be such that it does not interfere with the ability of the a domain to fold into a disulfide bonded structure. The class I β chain, β<sub>2</sub>-microglobulin, lacks a transmembrane domain in its native form, and need not be truncated. Generally, no Class II subunits will be used in conjunction with Class I subunits. Soluble class II subunits will include the  $\alpha 1$  and  $\alpha 2$  domains for the  $\alpha$  subunit, and the  $\beta 1$  and  $\beta 2$  domains for the  $\beta$ subunit. Not more than about 10, usually not more than about 5, preferably none of the amino acids of the transmembrane domain will be included. The deletion may extend as much as about 10 amino acids into the  $\alpha 2$  or  $\beta 2$  domain, preferably none of the amino acids of the \beta2 or \beta2 domain will be deleted. The deletion will be such that it does not interfere with the ability of the  $\alpha 2$  or  $\beta 2$  domain to fold into a disulfide bonded structure.

[0067] The monomeric complex  $(\alpha-\beta-P)$  (monomer) is multimerized. The resulting multimer will be stable over long periods of time. Usually not more than about 10% of the multimer will be dissociated after storage at 4° C for about one day, more usually after about one week. Preferably, the multimer will be formed by binding the monomers to a multivalent entity through specific attachment sites on the  $\alpha$  or  $\beta$  subunit, as described below in detail. The multimer may also be formed by chemical cross-linking of the monomers. A number of reagents capable of cross-linking proteins are known in azidobenzoyl hydrazide, include: N-[4-(pthe art, illustrative entities bis-sulfosuccinimidyl azidosalicylamino)butyl]-3'-[2'-pyridyldithio]propionamide), disuccinimidyltartrate, N-.gamma.suberate, dimethyladipimidate, maleimidobutyryloxysuccinimide ester, N-hydroxy sulfosuccinimidyl-4-azidobenzoate,



[4-azidophenyl]-1,3'-dithiopropionate, N-succinimidyl [4-N-succinimidyl iodoacetyl]aminobenzoate, glutaraldehyde, formaldehyde and succinimidyl 4-Mmaleimidomethyl]cyclohexane-1-carboxylate.

[0068] The attachment site for binding to a multivalent entity may be naturally occurring, or may be introduced through genetic engineering. The site will be a specific binding pair member or one that is modified to provide a specific binding pair member, where the complementary pair has a multiplicity of specific binding sites. Binding to the complementary binding member can be a chemical reaction, epitope-receptor binding or hapten-receptor binding where a hapten is linked to the subunit chain. In a preferred embodiment, one of the subunits is fused to an amino acid sequence providing a recognition site for a modifying enzyme. The recognition sequence will usually be fused proximal to the carboxy terminus of one of the subunit to avoid potential hindrance at the antigenic peptide binding site. Conveniently, an expression cassette will include the sequence encoding the recognition site.

[0069] Modifying enzymes of interest include BirA, various glycosylases, farnesyl protein transferase, protein kinases and the like. The subunit may be reacted with the modifying enzyme at any convenient time, usually after formation of the monomer. The group introduced by the modifying enzyme, e.g. biotin, sugar, phosphate, farnesyl, etc. provides a complementary binding pair member, or a unique site for further modification, such as chemical cross-linking, biotinylation, etc. that will provide a complementary binding pair member. An alternative strategy is to introduce an unpaired cysteine residue to the subunit, thereby introducing a unique and chemically reactive site for binding. The attachment site may also be a naturally occurring or introduced epitope, where the multivalent binding partner will be an antibody, e.g. IgG, IgM, etc. Any modification will be at a site, e.g. C-terminal proximal, that will not interfere with binding.

[0070] Exemplary of multimer formation is the introduction of the recognition sequence for the enzyme BirA, which catalyzes biotinylation of the protein substrate. The monomer with a biotinylated subunit is then bound to a multivalent binding partner, e.g. streptavidin or avidin, to which biotin binds with extremely high affinity. Streptavidin has a valency of 4, providing a multimer of  $(\alpha-\beta-P)_4$ .



[0071] The multivalent binding partner may be free in solution, or may be attached to an insoluble support. Examples of suitable insoluble supports include beads, e.g. magnetic beads, membranes and microtiter plates. These are typically made of glass, plastic (e.g. polystyrene), polysaccharides, nylon or nitrocellulose. Attachment to an insoluble support is useful when the binding complex is to be used for separation of T cells.

[0072] Frequently, the multimeric complex will be labeled, so as to be directly detectable, or will be used in conjunction with secondary labeled immunoreagents which will specifically bind the complex. In general the label will have a light detectable characteristic. Preferred labels are fluorophors, such as fluorescein isothiocyanate (FITC), rhodamine, Texas Red, phycoerythrin and allophycocyanin. Other labels of interest may include dyes, enzymes, chemiluminescers, particles, radioisotopes, or other directly or indirectly detectable agent. Conveniently, the multivalent binding partner will have the labeling group. Alternatively, a second stage label may be used, e.g. labeled antibody directed to one of the peptide constituents, and the like.

[0073] The binding complex will be used to detect and/or separate antigen specific T cells. The T cells may be from any source, usually having the same species of origin as the MHC heterodimer. The T cells may be from an in vitro culture, or a physiologic sample. For the most part, the physiologic samples employed will be blood or lymph, but samples may also involve other sources oft cells, particularly where T cells may be invasive. Thus other sites of interest are tissues, or associated fluids, as in the brain, lymph node, neoplasms, spleen, liver, kidney, pancreas, tonsil, thymus, joints, synovia, and the like. The sample may be used as obtained or may be subject to modification, as in the case of dilution, concentration, or the like. Prior treatments may involve removal of cells by various techniques, including centrifugation, using Ficoll-Hypaque, panning, affinity separation, using antibodies specific for one or more markers present as surface membrane proteins on the surface of cells, or any other technique that provides enrichment of the set or subset of cells of interest.

[0074] The binding complex is added to a suspension comprising T cells of interest, and incubated at about 4° C for a period of time sufficient to bind the available cell surface receptor. The incubation will usually be at least about 5 minutes and usually

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less than about 30 minutes. It is desirable to have a sufficient concentration of labeling reagent in the reaction mixture, so that labeling reaction is not limited by lack of labeling reagent. The appropriate concentration is determined by titration. The medium in which the cells are labeled will be any suitable medium as known in the art. If live cells are desired a medium will be chosen that maintains the viability of the cells. A preferred medium is phosphate buffered saline containing from 0.1 to 0.5% BSA. Various media are commercially available and may be used according to the nature of the cells, including Dulbecco's Modified Eagle Medium (dMEM), Hank's Basic Salt Solution (HBSS), Dulbecco's phosphate buffered saline (dPBS), RPMI, Iscove's medium, PBS with 5 mM EDTA, etc., frequently supplemented with fetal calf serum, BSA, HSA, etc.

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[0075] Where a second stage labeling reagent is used, the cell suspension may be washed and resuspended in medium as described above prior to incubation with the second stage reagent. Alternatively, the second stage reagent may be added directly into the reaction mix.

[0076] A number of methods for detection and quantitation of labeled cells are known in the art. Flow cytometry is a convenient means of enumerating cells that are a small percent of the total population. Fluorescent microscopy may also be used. Various immunoassays, e.g. ELISA, RIA, etc. may used to quantitate the number of cells present after binding to an insoluble support.

[0077] Flow cyometry may also be used for the separation of a labeled subset of T cells from a complex mixture of cells. The cells may be collected in any appropriate medium which maintains the viability of the cells, usually having a cushion of serum at the bottom of the collection tube. Various media are commercially available as described above. The cells may then be used as appropriate.

[0078] Alternative means of separation utilize the binding complex bound directly or indirectly to an insoluble support, e.g. column, microtiter plate, magnetic beads, etc. The cell sample is added to the binding complex. The complex may be bound to the support by any convenient means. After incubation, the insoluble support is washed to remove non-bound components. From one to six washes may be employed, with sufficient volume to thoroughly wash non-specifically bound cells present in the sample. The desired cells are then eluted from the binding complex. In particular the use of



magnetic particles to separate cell subsets from complex mixtures is described in Miltenyi et al. (1990) Cytometry 11:231-238.

[0079] Detecting and/or quantitating specific T cells in a sample or fraction thereof may be accomplished by a variety of specific assays. In general, the assay will measure the binding between a patient sample, usually blood derived, generally in the form of plasma or serum and the subject multimeric binding complexes. The patient sample may be used directly, or diluted as appropriate, usually about 1:10 and usually not more than about 1:10,000. Assays may be performed in any physiological buffer, e.g. PBS, normal saline, HBSS, dPBS, etc.

[0080] A sandwich assay is performed by first attaching the multimeric binding complex to an insoluble surface or support. The multimeric binding complex may be bound to the surface by any convenient means, depending upon the nature of the surface, either directly or through specific antibodies. The particular manner of binding is not crucial so long as it is compatible with the reagents and overall methods of the invention. They may be bound to the plates covalently or non-covalently, preferably non-covalently.

[0081] The insoluble supports may be any compositions to which the multimeric binding complex can be bound, which is readily separated from soluble material, and which is otherwise compatible with the overall method of measuring T cells. The surface of such supports may be solid or porous and of any convenient shape. Examples of suitable insoluble supports to which the receptor is bound include beads, e.g. magnetic beads, membranes and microtiter plates. These are typically made of glass, plastic (e.g. polystyrene), polysaccharides, nylon or nitrocellulose. Microtiter plates are especially convenient because a large number of assays can be carried out simultaneously, using small amounts of reagents and samples.

[0082] Before adding patient samples or fractions thereof, the non-specific binding sites on the insoluble support i.e. those not occupied by the multimeric binding complex, are generally blocked. Preferred blocking agents include non-interfering proteins such as bovine serum albumin, casein, gelatin, and the like. Samples, fractions or aliquots thereof are then added to separately assayable supports (for example, separate wells of a microtiter plate) containing support-bound multimeric binding complex.

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[0083] Generally from about 0.001 to 1 ml of sample, diluted or otherwise, is sufficient, usually about 0.01 ml sufficing. Preferably, each sample and standard will be added to multiple wells so that mean values can be obtained for each. The incubation time should be sufficient for T cells to bind the insoluble binding complex. Generally, from about 0.1 to 3 hr is sufficient, usually 1 hr sufficing.

[0084] After incubation, the insoluble support is generally washed of non-bound components. Generally, a dilute physiologic buffer at an appropriate pH, generally 7-8, is used as a wash medium. From one to six washes may be employed, with sufficient volume to thoroughly wash non-specifically bound T cells present in the sample.

[0085] After washing, a solution containing specific second receptor is applied. The receptor may be any compound that binds patient T cells with sufficient specificity such that they can be distinguished from other components present. In a preferred embodiment, second receptors are antibodies specific for common T cell antigens, either monoclonal or polyclonal sera, e.g. anti-thy-1, anti-CD45, etc.

[0086] T cell specific antibodies may be labeled to facilitate direct or indirect quantification of binding. Examples of labels that permit direct measurement include radiolabels, such as <sup>3</sup>H or <sup>125</sup>I, fluorescers, dyes, beads, chemilumninescers, colloidal particles, and the like. Examples of labels which permit indirect measurement of binding include enzymes where the substrate may provide for a colored or fluorescent product. Examples of suitable enzymes for use in conjugates include horseradish peroxidase, alkaline phosphatase, malate dehydrogenase and the like. Where not commercially available, such antibody-enzyme conjugates are readily produced by techniques known to those skilled in the art.

[0087] Alternatively, the second receptor may be unlabeled. In this case, a labeled second receptor-specific compound is employed which binds to the bound second receptor. Such a second receptor-specific compound can be labelled in any of the above manners. It is possible to select such compounds such that multiple compounds bind each molecule of bound second receptor. Examples of second receptor/second receptor-specific molecule pairs include antibody/anti-antibody and avidin (or streptavidin)/biotin. Since the resultant signal is thus amplified, this technique may be advantageous where only a small number oft cells are present. An example is the use of a labeled antibody

rodentia, particularly mouse, or bovine.

specific to the second receptor. More specifically, where the second receptor is a rabbit anti-allotypic antibody, an antibody directed against the constant region of rabbit antibodies provides a suitable second receptor specific molecule. The anti-

[0088] The volume, composition and concentration of T cell specific receptor solution provides for measurable binding to the T cells already bound to the insoluble substrate. Generally, the same volume as that of the sample is used: from about 0.001 to 1 ml is sufficient, usually about 0.1 ml sufficing. When antibody ligands are used, the concentration generally will be about 0.1 to 50 µg/ml, preferably about 1 µg/ml. The solution containing the second receptor is generally buffered in the range of about pH 6.5-9.5. The solution may also contain an innocuous protein as previously described. The incubation time should be sufficient for the labeled ligand to bind available molecules. Generally, from about 0.1 to 3 hr is sufficient, usually 1 hr sufficing.

immunoglobulin will usually come from any source other than human, such as ovine,

[0089] After the second receptor or second receptor-conjugate has bound, the insoluble support is generally again washed free of non-specifically bound second receptor, essentially as described for prior washes. After non-specifically bound material has been cleared, the signal produced by the bound conjugate is detected by conventional means. Where an enzyme conjugate is used, an appropriate enzyme substrate is provided so a detectable product is formed. More specifically, where a peroxidase is the selected enzyme conjugate, a preferred substrate combination is  $H_2O_2$  and O-phenylenediamine which yields a colored product under appropriate reaction conditions. Appropriate substrates for other enzyme conjugates such as those disclosed above are known to those skilled in the art. Suitable reaction conditions as well as means for detecting the various useful conjugates or their products are also known to those skilled in the art. For the product of the substrate O-phenylenediamine for example, light absorbance at 490-495 nm is conveniently measured with a spectrophotometer.

[0090] Generally the number of bound T cells detected will be compared to control samples from samples having a different MHC context, e.g. T cells from an animal that does not express the MHC molecule used to make the binding complex.



[0091] An alternative protocol is to provide anti-T cell reagent, e.g. anti-thy-1, anti-CD45, etc. bound to the insoluble surface. After adding the sample and washing away non-specifically bound T cells, one or a combination of the subject binding complexes are added, where the binding complexes are labeled so as not to interfere with the binding to T cells.

[0092] It is particularly convenient in a clinical setting to perform the assays in a self-contained apparatus. A number of such methods are known in the art. The apparatus will generally employ a continuous flow-path of a suitable filter or membrane, having at least three regions, a fluid transport region, a sample region, and a measuring region. The sample region is prevented from fluid transfer contact with the other portions of the flow path prior to receiving the sample. After the sample region receives the sample, it is brought into fluid transfer relationship with the other regions, and the fluid transfer region contacted with fluid to permit a reagent solution to pass through the sample region and into the measuring region. The measuring region may have bound to it the multimeric binding complex, with a conjugate of an enzyme with T cell specific antibody employed as a reagent, generally added to the sample before application. Alternatively, the binding complex may be conjugated to an enzyme, with T cell specific antibody bound to the measurement region.

[0093] Detection of T cells is of interest in connection with a variety of conditions associated with T cell activation. Such conditions include autoimmune diseases, e.g. multiple sclerosis, myasthenia gravis, rheumatoid arthritis, type 1 diabetes, graft vs. host disease, Grave's disease, etc.; various forms of cancer, e.g. carcinomas, melanomas, sarcomas, lymphomas and leukemias. Various infectious diseases such as those caused by viruses, e.g. HIV-1, hepatitis, herpesviruses, enteric viruses, respiratory viruses, rhabdovirus, rubeola, poxvirus, paramyxovirus, morbillivirus, etc. are of interest. Infectious agents of interest also include bacteria, such as Pneumococcus, Staphylococcus, Bacillus. Streptococcus, Meningococcus, Gonococcus, Eschericia, Klebsiella, Proteus, Pseudomonas, Salmonella, Shigella, Hemophilus, Yersinia, Listeria, Corynebacterium, Vibrio, Clostridia, Chlamydia, Mycobacterium, Helicobacter and Treponema; protozoan pathogens, and the like. T cell associated allergic responses may also be monitored, e.g. delayed type hypersensitivity or contact hypersensitivity involving T cells.



[0094] Of particular interest are conditions having an association with a specific peptide or MHC haplotype, where the subject binding complexes may be used to track the T cell response with respect to the haplotype and antigen. A large number of associations have been made in disease states that suggest that specific MHC haplotypes, or specific protein antigens are responsible for disease states.

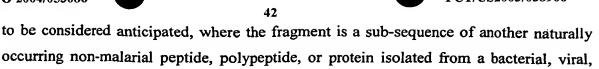
[0095] Polypeptide fragments, including immunogenic fragments, for each of SEQ ID NOs: 1-27 can be any length from at least 5 consecutive amino acids to 1 amino acid less than a full length polypeptide of any given SEQ ID NO:. Thus, for SEQ ID NO: 1 (used here as a non-limiting example) the polypeptide fragment can contain any number of consecutive amino acids from 5 to 1903 (for example, 5, 6, 7, ..., 1901, 1902, 1903). For the sake of brevity, the individual integers between 5 and 1903 have not been reproduced herein but are, in fact, specifically contemplated. In one embodiment, the immunogenic fragments of the invention induce immunity or protective immunity from disease.

[0096] The present invention also provides for the exclusion of any individual fragment (of any given SEQ ID NO:) specified by N-terminal to C-terminal positions, actual sequence, or of any fragment specified by size (in amino acid residues) as described above. In addition, any number of fragments specified by N-terminal and C-terminal positions, actual sequence, or by size (in amino acid residues) as described above may be excluded as individual species. Further, any number of fragments specified by N-terminal and C-terminal positions or by size (in amino acid residues) as described above may be combined to provide a polypeptide fragment. These types of fragments may, optionally, include polypeptide sequences such as linkers, described below.

[0097] Where a claim recites "a polypeptide comprising SEQ ID NO: X, or fragments or immunogenic fragments or epitopes of SEQ ID NO:X", the language "fragments or immunogenic fragments or epitopes of SEQ ID NO:X" specifically excludes identical sub-sequences found within other longer naturally occurring prior art polypeptide or protein sequences that are not identical to sequence from which the claimed sequence was derived. This does not include instances where such sub-sequences are a part of a larger molecule specifically modified by the hand of man to enhance the immunogenicity of the fragments of the subject invention. Thus, fragments or immunogenic fragments or epitopes of SEQ ID NO:X specifically exclude, and are not

sequence databases.

reptilian, insect, avian, or mammalian source and is identified in a search of protein



[0098] Fragments or immunogenic fragments or epitopes of the invention may further contain linkers that facilitate the attachment of the fragments to a carrier molecule for the stimulation of an immune response or diagnostic purposes. The linkers can also be used to attach fragments according to the invention to solid support matrices for use in affinity purification protocols. In this aspect of the invention, the linkers specifically exclude, and are not to be considered anticipated, where the fragment is a subsequence of another peptide, polypeptide, or protein as identified in a search of protein sequence databases as indicated in the preceding paragraph. In other words, the non-identical portions of the other peptide, polypeptide, of protein are not considered to be a "linker" in this aspect of the invention. Non-limiting examples of "linkers" suitable for the practice of the invention include chemical linkers (such as those sold by Pierce, Rockford, IL) and peptides that allow for the connection of the immunogenic fragment to a carrier molecule (see, for example, linkers disclosed in U.S. Patent Nos. 6,121,424, 5,843,464, 5,750,352, and 5,990,275, hereby incorporated by reference in their entirety). embodiments, the linkers can be up to 50 amino acids in length, up to 40 amino acids in length, up to 30 amino acids in length, up to 20 amino acids in length, up to 10 amino acids in length, or up to 5 amino acids in length. Of course, the linker may be any preselected number of amino acids (up to 50 amino acids) in length.

[0099] In various embodiments, polypeptides suitable for use in various disclosed methods of the subject invention can be selected from the group consisting of: a) a polypeptide comprising a polypeptide sequence selected from the group consisting of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27; b) a variant polypeptide having at least about 20% to 99.99% identity to a polypeptide selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27; c) a fragment of a polypeptide or a variant polypeptide of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, or 27, wherein said fragment or variant



has substantially the same serologic reactivity or substantially the same T-cell reactivity as the native polypeptide; d) a multi-epitope construct; and e) combinations thereof.

## Multi-epitope constructs

[00100] As indicated *supra*, the subject invention provides for "multi-epitope constructs". A "multi-epitope construct" comprises: 1) nucleic acids that encode multiple polypeptide epitopes (of any length) that can bind to one or more molecules functioning in the immune system; or 2) polypeptides comprising multiple polypeptide epitopes that can bind to one or more molecules functioning in the immune system. "Multi-epitope constructs" can, optionally, contain "flanking" or "spacing" residues between each epitope. Some embodiments provide for "multi-epitope constructs" that comprise a series of the same epitope (termed "homopolymers"). Other embodiments provide for "multiepitope constructs" that comprise a combination or series of different epitopes, optionally connected by "flanking" or "spacing" residues (termed "heteropolymers"). In some embodiments, "multi-epitope constructs" may exclude full-length polypeptides from which the epitopes are obtained (e.g., the polypeptides of SEQ ID NOs: 1-27). In certain preferred embodiments, the epitopes used in the formation of the multi-epitope construct are selected from those set forth in Table 2, Table 3, Table 4, Table 5, and/or Table 6 and any epitope set forth in these Tables 2-6 can be mixed and/or matched any other epitope set forth in any of the aforementioned Tables 2-6.

[00101] Multi-epitope constructs may be of "high affinity" or "intermediate affinity". As used herein, "high affinity" with respect to HLA class I molecules is defined as binding with an IC<sub>50</sub>, or KD value, of 50 nM or less; "intermediate affinity" with respect to HLA class I molecules is defined as binding with an IC50 or KD value of between about 50 and about 500 nM. "High affinity" with respect to binding to HLA class II molecules is defined as binding with an IC<sub>50</sub> or KD value of 100 nM or less; "intermediate affinity" with respect to binding to HLA class II molecules is defined as binding with an IC<sub>50</sub> or KD value of between about 100 and about 1000 nM.

[00102] The multi-epitope constructs described herein preferably include five or more, ten or more, fifteen or more, twenty or more, or twenty-five or more epitopes. Other embodiments provide multi-epitope constructs that comprise at least 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33,



34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99 epitopes. All of the epitopes in a multi-epitope construct may be from one organism (e.g., the epitopes are obtained from P. falciparum), or the multi-epitope construct may include epitopes present in two or more different organisms (e.g., some epitopes from P. falciparum and some epitopes from another organism). Additionally, the same epitope may be present in a multi-epitope construct at more than one location in the construct. In some embodiments, novel epitopes of the subject invention may be linked to known epitopes of an organism (e.g., P. falciparum or another organism).

[00103] A "multi-epitope vaccine," is a vaccine comprising multiple epitopes. A multi-epitope vaccine can induce an immune response and is administered to an individual in an amount sufficient to induce an immune response in the individual. In some embodiments, the immune response induced by the multi-epitope vaccine is a protective immune response against a given organism, pathogen, or pathologic condition (e.g., P. falciparum).

[00104] In certain embodiments, the epitopes of a multi-epitope construct or the polypeptides disclosed herein interact with an antigen binding site of an antibody molecule, a class I HLA, a T-cell receptor, and/or a class II HLA molecule. In certain preferred embodiments, the epitopes interact with an HLA molecule (e.g., class I or class II) or a T-cell receptor. In an even more preferred embodiment, the epitope interacts with both an HLA molecule (e.g., class I or class II) and a T-cell receptor. In various embodiments, all of the nucleic acids in a multi-epitope construct can encode class I HLA epitopes or class II HLA epitopes. Multi-epitope constructs comprising epitopes that interact exclusively with class I HLA molecules may be referred to as "CTL multiepitope constructs" (or "CD8<sup>+</sup> T cell multi-epitope constructs"). Multi-epitope constructs comprising epitopes that interact exclusively with class II HLA molecules may be referred to as "HTL multi-epitope constructs" (or "CD4" T cell multi epitope constructs"). Some multi-epitope constructs (designated "TL multi-epitope constructs") can have a subset of the multi-epitope nucleic acids encoding class I HLA epitopes and another subset of the multi-epitope nucleic acids encoding class II HLA epitopes (e.g., the constructs stimulate both CTL (i.e., CD8<sup>+</sup> T cell) and HTL (i.e., CD4<sup>+</sup> T cell) of the immune system). Other multi-epitope constructs can provide epitopes that interact exclusively with B-cells or immunoglobulin molecules and are designated "BL multi-epitope constructs". Multi-epitope constructs that provide epitopes that interact with B-cells (and/or immunoglobulin molecules) and further provide class I HLA epitopes and class II HLA epitopes are designated "immune system (IMS) multi-epitope constructs". In certain embodiments, multi-epitope constructs can provide class I or class II epitopes (e.g., CTL (i.e., CD8<sup>+</sup> T cell) epitopes or HTL (i.e., CD4<sup>+</sup> T cell) epitopes) and BL epitopes. "Human Leukocyte Antigen" or "HLA" is a human class I or class II Major Histocompatibility Complex (MHC) protein (see, e.g., Stites, et al., IMMUNOLOGY, 8<sup>TH</sup> ED., Lange Publishing, Los Altos, Calif. (1994)).

[00105] CTL epitope (class I epitope) (i.e., CD8<sup>+</sup> T cell epitope) encoding nucleic acids preferably provide an epitope peptide of about eight to about thirteen amino acids in length (e.g., 8, 9, 10, 11, 12 or 13), more preferably about eight to about eleven amino acids in length, and most preferably about nine amino acids in length. HTL (CD4<sup>+</sup> T-cell) epitope nucleic acids can provide an epitope peptide of about seven to about twenty three (e.g., 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22 or 23) preferably about seven to about seventeen (e.g., 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or 17, more preferably about eleven to about fifteen (e.g., 11, 12, 13, 14 or 15), and most preferably about thirteen amino acids in length.

[00106] "Degenerate binding" indicates that a peptide is bound by more than one HLA molecule; a synonym is "cross reactive binding." "Cross reactive binding" may also be used to define the interaction of an antigen with multiple populations of antibodies. In certain preferred embodiments, epitopes disclosed herein do not exhibit cross reactive or degenerate binding. Other embodiments encompass degenerate or cross reactive binding of antigens or epitopes.

[00107] With regard to a particular amino acid sequence, an "epitope" is a set of amino acid residues that is involved in recognition by a particular immunoglobulin, or in the context of T cells, those residues necessary for recognition by T cell receptor proteins and/or Major Histocompatibility Complex (MHC) receptors. In an immune system setting, in vitro or in vivo, an epitope is the collective features of a molecule, such as primary, secondary and tertiary peptide structure, and charge, that together form a site recognized by an immunoglobulin, T cell receptor or HLA molecule. Throughout this

disclosure epitope and peptide are often used interchangeably. It is to be appreciated, however, that isolated or purified protein or peptide molecules larger than and comprising an epitope of the invention are still within the bounds of the invention.

[00108] A "flanking" or "linking" residue is a residue that is positioned next to an epitope. A flanking residue can be introduced or inserted at a position adjacent to the N-terminus or the C-terminus of an epitope. Flanking residues suitable for use in the subject invention are disclosed, for example, in U.S. Patent Nos. 6,419,931, which is hereby incorporated by reference in its entirety, including all sequences, figures, references, and tables.

[00109] An "immunogenic peptide" or "peptide epitope" is a peptide that comprises an allele-specific motif or supermotif such that the peptide will bind an HLA molecule and induce a CTL (or CD8<sup>+</sup> T cell) and/or HTL (or CD4<sup>+</sup> T cell) response. An "immunogenic peptide" or "peptide epitope" can also be a peptide that comprises a motif that binds to antibody molecules or B-cells found in the immune system of an individual. Thus, immunogenic peptides of the invention are capable of binding to an antibody molecule, a B-cell, or appropriate HLA molecule and thereafter inducing an immune response (e.g., the induction of antibody production, a cytotoxic T cell response, or a helper T cell response) to the antigen from which the immunogenic peptide is derived.

- [00110] The term "residue" refers to an amino acid or amino acid mimetic incorporated into a peptide or protein by an amide bond or amide bond mimetic.
- [00111] A "spacer" or "linker" refers to a sequence that is inserted between two epitopes in a multi-epitope construct to prevent the occurrence of junctional epitopes and/or to increase the efficiency of processing. A multi-epitope construct may have one or more spacer nucleic acids. A spacer nucleic acid may flank each epitope nucleic acid in a construct, or the spacer nucleic acid to epitope nucleic acid ratio may be about 2 to 10, about 5 to 10, about 6 to 10, about 7 to 10, about 8 to 10, or about 9 to 10, where a ratio of about 8 to 10 has been determined to yield favorable results for some constructs. The spacer nucleic acid may encode one or more amino acids. A spacer nucleic acid flanking a class I HLA epitope in a multi-epitope construct is preferably between one and about eight amino acids in length. A spacer nucleic acid flanking a class II HLA epitope in a multi-epitope construct is preferably greater than five, six, seven, or more amino acids in



length, and more preferably five or six amino acids in length. The number of spacers in a construct, the number of amino acids in a spacer, and the amino acid composition of a spacer can be selected to optimize epitope processing and/or minimize junctional epitopes. It is preferred that spacers are selected by concomitantly optimizing epitope processing and junctional motifs. Suitable amino acids for optimizing epitope processing are described herein. Also, suitable amino acid spacing for minimizing the number of junctional epitopes in a construct are described herein for class I and class II HLAs. For example, spacers flanking class II HLA epitopes preferably include G, P, and/or N residues as these are not generally known to be primary anchor residues (see, e.g., PCT/US00/19774). A particularly preferred spacer for flanking a class II HLA epitope includes alternating G and P residues, for example, (GP)<sub>n</sub>, (PG)<sub>n</sub>, (GP)<sub>n</sub>G, or (PG)<sub>n</sub>P, and so forth, where n is an integer between one and ten, preferably two or about two, and where a specific example of such a spacer is GPGPG.

[00112] In some multi-epitope constructs, it is sufficient that each spacer nucleic acid encodes the same amino acid sequence. In multi-epitope constructs having two spacer nucleic acids encoding the same amino acid sequence, the spacer nucleic acids encoding those spacers may have the same or different nucleotide sequences, where different nucleotide sequences may be preferred to decrease the likelihood of unintended recombination events when the multi-epitope construct is inserted into cells.

[00113] In other multi-epitope constructs, one or more of the spacer nucleic acids may encode different amino acid sequences. While many of the spacer nucleic acids may encode the same amino acid sequence in a multi-epitope construct, one, two, three, four, five or more spacer nucleic acids may encode different amino acid sequences, and it is possible that all of the spacer nucleic acids in a multi-epitope construct encode different amino acid sequences. Spacer nucleic acids may be optimized with respect to the epitope nucleic acids they flank by determining whether a spacer sequence will maximize epitope processing and/or minimize junctional epitopes, as described herein.

[00114] Multi-epitope constructs may be distinguished from one another according to whether the spacers in one construct optimize epitope processing or minimize junctional epitopes over another construct, and preferably, constructs may be distinguished where one construct is concomitantly optimized for epitope processing and junctional epitopes over the other. Computer assisted methods and in vitro and in vivo



laboratory methods for determining whether a construct is optimized for epitope processing and junctional motifs are described herein.

[00115] "Multi-epitope constructs of the invention may also be "optimized". The term "optimized" or "optimizing" refers to increasing the immunogenicity or antigenicity of a multi-epitope construct having at least one epitope pair by sorting epitopes to minimize the occurrence of junctional epitopes, inserting flanking residues that flank the C-terminus or N-terminus of an epitope, and inserting spacer residue to further prevent the occurrence of junctional epitopes or to provide a flanking residue. An increase in immunogenicity or antigenicity of an optimized multi-epitope construct is measured relative to a multi-epitope construct that has not been constructed based on the optimization parameters and is using assays known to those of skill in the art, e.g., assessment of immunogenicity in HLA transgenic mice, ELISPOT, interferon-gamma release assays, tetramer staining, chromium release assays, and presentation on dendritic cells.

[00116] The subject invention also concerns antibodies that bind to polypeptides of the invention. Antibodies that are immunospecific for the malarial polypeptides set forth herein are specifically contemplated. In various embodiments, antibodies which do not cross react with other proteins or malarial proteins are also specifically contemplated. The antibodies of the subject invention can be prepared using standard materials and methods known in the art (see, for example, Monoclonal Antibodies: Principles and Practice, 1983; Monoclonal Hybridoma Antibodies: Techniques and Applications, 1982; Selected Methods in Cellular Immunology, 1980; Immunological Methods, Vol. II, 1981; Practical Immunology, and Kohler et al. [1975] Nature 256:495).

[00117] The term "antibody" is used in the broadest sense and specifically covers monoclonal antibodies (including full length monoclonal antibodies), polyclonal antibodies, multispecific antibodies (e.g., bispecific antibodies), and antibody fragments so long as they exhibit the desired biological activity, particularly neutralizing activity. "Antibody fragments" comprise a portion of a full length antibody, generally the antigen binding or variable region thereof. Examples of antibody fragments include Fab, Fab', F(ab')2, and Fv fragments; diabodies; linear antibodies; single-chain antibody molecules; and multi-specific antibodies formed from antibody fragments.



[00118] The term "monoclonal antibody" as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the individual antibodies comprising the population are identical except for possible naturally occurring mutations that may be present in minor amounts. Monoclonal antibodies are highly specific, being directed against a single antigenic site. Furthermore, in contrast to conventional (polyclonal) antibody preparations that typically include different antibodies directed against different determinants (epitopes), each monoclonal antibody is directed against a single determinant on the antigen. The modifier "monoclonal" indicates the character of the antibody as being obtained from a substantially homogeneous population of antibodies, and is not to be construed as requiring production of the antibody by any particular method. For example, the monoclonal antibodies to be used in accordance with the present invention may be made by the hybridoma method first described by Kohler et al. [1975] Nature 256: 495, or may be made by recombinant DNA methods (see, e.g., U.S. Pat. No. 4,816,567). The "monoclonal antibodies" may also be isolated from phage antibody libraries using the techniques described in Clackson et al. [1991] Nature 352: 624-628 and Marks et al. [1991] J. Mol. Biol. 222: 581-597, for example.

[00119] The monoclonal antibodies described herein specifically include "chimeric" antibodies (immunoglobulins) in which a portion of the heavy and/or light chain is identical with or homologous to corresponding sequences in antibodies derived from a particular species or belonging to a particular antibody class or subclass, while the remainder of the chain(s) is identical with or homologous to corresponding sequences in antibodies derived from another species or belonging to another antibody class or subclass, as well as fragments of such antibodies, so long as they exhibit the desired biological activity (U.S. Pat. No. 4,816,567; and Morrison et al. [1984] Proc. Natl. Acad Sci. USA 81: 6851-6855). Also included are humanized antibodies, such as those taught in U.S. Patent Nos. 6,407,213 or 6,417,337 which are hereby incorporated by reference in their entirety.

[00120] "Single-chain Fv" or "sFv" antibody fragments comprise the  $V_H$  and  $V_L$  domains of an antibody, wherein these domains are present in a single polypeptide chain. Generally, the Fv polypeptide further comprises a polypeptide linker between the  $V_H$  and  $V_L$  domains which enables the sFv to form the desired structure for antigen binding. For

a review of sFv see Pluckthun in The Pharmacology of Monoclonal Antibodies [1994] Vol. 113:269-315, Rosenburg and Moore eds. Springer-Verlag, New York.

[00121] The term "diabodies" refers to small antibody fragments with two antigen-binding sites, which fragments comprise a heavy chain variable domain (V<sub>H</sub>) connected to a light chain variable domain (V<sub>L</sub>) in the same polypeptide chain (V<sub>H</sub> -V<sub>L</sub>). Diabodies are described more fully in, for example, EP 404,097; WO 93/11161; and Hollinger et al. [1993] Proc. Natl. Acad. Sci. USA 90: 6444-6448. The term "linear antibodies" refers to the antibodies described in Zapata et al. [1995] Protein Eng. 8(10):1057-1062.

[00122] An "isolated" antibody is one which has been identified and separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials which would interfere with diagnostic or therapeutic uses for the antibody, and may include enzymes, hormones, and other proteinaceous or nonproteinaceous solutes. In preferred embodiments, the antibody will be purified (1) to greater than 95% by weight of antibody as determined by the Lowry method, and most preferably more than 99% by weight, (2) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (3) to homogeneity by SDS-PAGE under reducing or nonreducing conditions using Coomassie blue or, preferably, silver stain. Isolated antibody includes the antibody in situ within recombinant cells since at least one component of the antibody will be prepared by at least one purification step.

[00123] The terms "comprising", "consisting of" and "consisting essentially of" are defined according to their standard meaning. The terms may be substituted for one another throughout the instant application in order to attach the specific meaning associated with each term. The phrases "isolated" or "biologically pure" refer to material that is substantially or essentially free from components which normally accompany the material as it is found in its native state. Thus, isolated peptides in accordance with the invention preferably do not contain materials normally associated with the peptides in their *in situ* environment. "Link" or "join" refers to any method known in the art for functionally connecting peptides, including, without limitation, recombinant fusion,

covalent bonding, disulfide bonding, ionic bonding, hydrogen bonding, and electrostatic bonding.

[00124] Following are examples which illustrate procedures for practicing the invention. These examples should not be construed as limiting. All percentages are by weight and all solvent mixture proportions are by volume unless otherwise noted.

[00125] In this disclosure, "binding data" results are often expressed in terms of "IC<sub>50</sub>'s." IC<sub>50</sub> is the concentration of peptide in a binding assay at which 50% inhibition of binding of a reference peptide is observed. Given the conditions in which the assays are run (i.e., limiting HLA proteins and labeled peptide concentrations), these values approximate KD values. Assays for determining binding are described in detail, e.g., in PCT publications WO 94/20127 and WO 94/03205 (each of which is hereby incorporated by reference in its entirety). It should be noted that IC<sub>50</sub> values can change, often dramatically, if the assay conditions are varied, and depending on the particular reagents used (e.g., HLA preparation, etc.). For example, excessive concentrations of HLA molecules will increase the apparent measured IC<sub>50</sub> of a given ligand. Alternatively, binding is expressed relative to a reference peptide. Although as a particular assay becomes more, or less, sensitive, the IC<sub>50</sub>'s of the peptides tested may change somewhat, the binding relative to the reference peptide will not significantly change. For example, in an assay run under conditions such that the IC<sub>50</sub> of the reference peptide increases 10fold, the IC<sub>50</sub> values of the test peptides will also shift approximately 10-fold. Therefore, to avoid ambiguities, the assessment of whether a peptide is a good, intermediate, weak, or negative binder is generally based on its  $IC_{50}$ , relative to the  $IC_{50}$  of a standard peptide. Binding may also be determined using other assay systems including those using: live cells (e.g., Ceppellini et al., Nature 339:392, 1989; Christnick et al., Nature 352:67, 1991; Busch et al., Int. Immunol. 2:443, 19990; Hill et al., J. Immunol. 147:189,1991; del Guercio et al., J. Immunol. 154:685, 1995), cell free systems using detergent lysates (e.g., Cerundolo et al., J. Immunol. 21:2069, 1991), immobilized purified MHC (e.g., Hill et al., J. Immunol. 152, 2890, 1994; Marshall et al., J. Immunol. 152:4946, 1994), ELISA systems (e.g., Reay et al., EMBO J. 11:2829, 1992), surface plasmon resonance (e.g., Khilko et al., J. Biol. Chem. 268:15425, 1993); high flux soluble phase assays (Hammer et al., J. Exp. Med. 180:2353, 1994), and measurement of class I MHC stabilization or assembly (e.g., Ljunggren et al., Nature 346:476, 1990; Schumacher et al., Cell 62:563, 1990; Townsend *et al.*, Cell 62:285, 1990; Parker *et al.*, J. Immunol. 149:1896, 1992). Predicted IC<sub>50</sub> values may be referred to as PIC values and measured IC<sub>50</sub> values may be referred to a MIC values.

## Example 1

[00126] Starting with 27 open reading frames defined by Multidimensional Protein Identification Technology, 9 highly antigenic proteins were identified. These highly antigenic proteins were recognized by volunteers immunized with irradiated sporozoites; mock immunized individuals (controls) failed to recognize these proteins. Several of these nine proteins were more antigenic than previously well-characterized proteins.

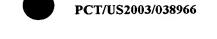
[00127] To identify and prioritize a set of ORFs representing antigens potentially expressed in the sporozoite and intrahepatic stage of the parasite life cycle, MS/MS spectra of peptide sequences generated by Multidimensional Protein Identification Technology (MudPIT) (Washburn, M.P., Wolters, D., & Yates, J.R. 3<sup>rd</sup>. Large-scale analysis of the yeast proteome by multidimensional protein identification technology. Nat. Biotechnol. 19, 242-247 (2001)) of P. falciparum sporozoite preparations were scanned against the P. falciparum genomic sequence database using SEQUEST<sup>TM</sup> software (Florens, L. et al. A proteomic view of the Plasmodium falciparum life cycle. Submitted). A panel of 27 ORF's (10 expressed only in sporozoites, and 17 common to other stages of the parasite life cycle) were selected. Their size ranged between 96 - 4544 amino acids (mean 1252), the percentage of the protein covered by identified peptides ranged between 0.5 - 49.5%, and the frequency of recognition in the P. falciparum proteome dataset ranged between 16 peptide hits from 6 different sporozoite runs (antigen 2) to single peptide hits (antigens 1, 11, 14, 16, 19 and 25. When searched against the final P. falciparum database using refined gene model predictions, and taking into consideration genomic sequence information from the Anopheles (vector) and human (host) databases, 19 of the 27 antigens could be identified using stringent selection criteria and six others could be identified only with relaxed criteria.

[00128] Amino acid sequences from the 27 ORFs were scanned with HLA-A1, A2, A3/A11, A24 and DR supertype PIC algorithms; a total of 3241 peptides were identified (range = 14-435; mean = 120 sequences per antigen). A set of 1142 sequences was synthesized (range = 13-50; mean = 42), selecting the top 10 scorers per supertype

EBV, HIV) were also included.

per antigen for larger ORFs. Control sets of peptides were synthesized from 4 known antigens (PfCSP, PfSSP2, PfLSA1 and PfEXP1). Next, predicted epitopes were tested for their capacity to induce recall IFN-γ immune responses using PBMC from volunteers immunized with irradiated *P. falciparum* sporozoites and either protected (n=4) or not protected (n=4) against challenge with infectious sporozoites, or control volunteers mock immunized in parallel (n=4) (see Table 1). Peptides were tested as pools, at 1 μg/ml each peptide with each antigen represented by a separate pool, by IFN-γ ELIspot (Washburn, M.P., Wolters, D., &Yates, J.R. 3<sup>rd</sup>. Large-scale analysis of the yeast proteome by multidimensional protein identification technology. *Nat. Biotechnol.* 19, 242-247 (2001)). Positive and negative control epitopes from well characterized antigens (CMV, Influenza,

[00129] Considering a stimulation index (ratio test response/control) > 2.0 as positive, 19 of the 27 unknown antigens were recognized by at least 1 of 8 irradiated sporozoite immunized volunteers, but not by any of the 4 mock immunized controls (Table 1). Nine of the 27 antigens (#2, 5, 3, 18, 22, 21, 13, 11, 20) were recognized by at least 50% of irradiated sporozoite volunteers in at least 25% of assays, 3 antigens (#1, 12, 17) were recognized by at least 25% of volunteers in at least 15% of assays, and 7 antigens (#6, 7, 9, 14, 15, 16, 19) were recognized by at least 10% volunteers in at least 5% of assays. Eight of the 27 unknown antigens (#4, 8, 10, 23, 24, 25, 26, 27) failed to induce IFN-y responses of sufficient magnitude to meet our criteria of positivity. Pools of predicted epitopes from the known antigens, PfCSP, PfSSP2, PfLSA1 and PfEXP1, were also recognized by irradiated sporozoite volunteers although the frequency of response to those pools was somewhat lower than that to pools of peptides representing previously validated epitopes derived from the same antigens (Doolan, D.L. et al. Degenerate cytotoxic T cell epitopes from P. falciparum restricted by multiple HLA-A and HLA-B supertype alleles. Immunity. 7, 97-112 (1997); Doolan, D.L. et al. HLA-DR-promiscuous T cell epitopes from Plasmodium flaciparum pre-erthrocytic-stage antigens restricted by multiple HLA class II alleles. J Immunol. 165:1123-1137 (2000); Wang, R., et al. Induction of CD4(+) T cell-dependent CD8(+) type 1 responses in humans by a malaria DNA vaccine. Proc. Natl. Acad. Sci. U.S.A. 98, 10817-10822 (2001)) (Table 1). Particularly noteworthy, the reactivity against several of the newly identified antigens greatly exceeded the reactivities observed against all 4 known antigens For example, both



antigens 2 and 5 were recognized by 7/8 irradiated sporozoite volunteers in 9/16 assays, and antigens 3 and 18 were recognized by 6/8 irradiated sporozoite volunteers in 6/16 assays.

[00130] Results show that HLA-A2 peptide pools from antigens 2, 5 and 13, and HLA-A1 and HLA-DR peptide pools from antigens 2 and 5, are recognized by irradiated sporozoite volunteers who express the respective HLA alleles, but not by mock immunized controls. Deconvolution at the level of individual epitopes is in progress. Additionally, a comprehensive analysis of HLA binding against the A1, A2, A3/11, A24, and DR1 supertypes has been completed for selected antigens. Several degenerate binders have been identified for each supertype/antigen combination, and 50 to 70% of the predicted peptides have been identified as degenerate HLA binders. Further analysis also revealed that the antigenicity results correlate to a large degree with the proteomic data. For example, of 9 antigens associated with high immune reactivity, 7 were identified by multiple peptide hits in multiple MudPIT runs

[00131] All patents, patent applications, provisional applications, polynucleotide sequences, amino acid sequences, tables and publications referred to or cited herein are incorporated by reference in their entirety, including all figures, to the extent they are not inconsistent with the explicit teachings of this specification. It should be understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to persons skilled in the art and are to be included within the spirit and purview of this application.

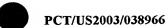


Table 1. Summary of immune reactivities against the panel of 27 putative antigens and 4 known antigens.

		IRRADIA	TED SPO	ROZOITE II	MMUNIZEI	)	MOO	
Antigen	# vol	% vol	#	%	SI	SFC	# vol	#
		respond	assays	assays	respond	respond	respond	assays
1	3	37.5	3	18.75	2.5	59.3	0	0
2	8	100	9	56.25	2.9	110.4	0	0
3	6	75	6	37.5	2.6	119.1	0	0
4	0	-	-	-	-	-	0	0
5	7	87.5	9	56.25	2.8	101.8	0	0
6	1	12.5	1	6.25	2.4	88.3	0	0
7	1	12.5	1	6.25	2.1	43.3	0	0
8	0	•	-	-	-	-	0	0
9	2	25	2	12.5	2.5	32.0	0	0
10	0	-	-	-	-	•	0	0
11	4	50	4	25	3.1	81.3	0	0
12	3	37.5	3	18.75	2.2	48.2	0	0
13	4	50	5	31.25	2.9	92.2	0	0
14	1	12.5	1	6.25	2.2	55.3	0	0
15	2	25	2	12.5	2.5	28.8	0	0
16	2	25	2	12.5	2.2	27.2	0	0
17	3	37.5	3	18.75	2.4	57.6	0	0
18	6	75	6	37.5	2.2	58.4	0	0
19	2	25	2	12.5	2.7	31.3	0	0
20	4	50	4	25	2.5	74.8	0	0
21	4	50	5	31.25	2.3	48.2	0	0
22	5	62.5	5	31.25	2.9	108.4	0	0
23	0	-	-	-	-	-	0	0
24	0	-	-	-	-	-	0	0 0
25	0	-	i -	-	-	-	0	0
26	0	-	-	-	-	-	0 0	0
27	0	-	-	-	2.5	66.6	<del>                                     </del>	
TOTAL UNKNOWNS	1-8	44.7	3.8	24.0			┪	
"HIGH"	4-8	66.7	5.9	36.8	2.7	88.3	1	
"INTERMEDIATE"	3	37.5	3.0	18.8	2.4	55.0 43.8		
"LOW"	1-2	19.6	1.6	9.8	2.4		-	
Range	1-8	12.5-100		6.25-56.25		27.2-110.4	-	
KNOWNS (@1ug/ml) predicted	1.4	17.2	1.4	8.6	2.9	57.3		
Range	1-3	12.5-37.5		6.25-18.75		30.5-137.4	4	
KNOWNS (@1ug/ml) validated	4.0	50.0	3.8	23.4	3.5	64.0		
Range	3-5	37.5-62.5		18.75-37.5	3.5-3.6 3.2	46.6-91.4 60.0	┨	
TOTAL KNOWNS (@1ug/ml)	2.3	28.1	2.2	13.5			.]	
Range	1-5	12.5-62.5		6.25-37.5	2.0-3.6	30.5-137.4	4	
TOTAL KNOWNS (@10ug/ml)		81.3	7.8	60.9	11.1	588.2	<del>]</del>	400
CMV/EBV/Flu	7	87.5	12.0	50.0	4.0	59.0	4	100

Table 2: Pf-derived A1 supertype peptides with PIC <20nM

A*2402 PIC	1000000.0	10000001	10000001	10000001	242.6	1753.1	10000001	10000000	1000000.0	1000000.0	10000000	10000000	1000000.0	1000000.0	1000000.0	1000000.0	1000000.0	10000000	1000000.0	10000000	1000000.0	1000000.0	10000000	1019.1	10000001	10000001	1000000.0	1000000.0
A*1101	1475.7	34.6	51.0	1000000.0	39035.2	10000000	153.7	4680.1	11308.4	4533.0	40.5	2464.4	445.2	22156.1	117.2	243.3	82.2	264.3	8368.7	4308.8	10911.0	698.4	150075.4	224.2	15763.1	6419.6	48.4	1000000.0
A*0201	1000000.0	10000001	10000000	10000001	10000001	1000000.0	1000000.0	10000000	10000000	10000001	0.0000001	10000000	10000001	10000001	10000001	10000000	1000000.0	10000001	10000001	1000000.0	10000000	10000001	1000000.0	1000000.0	10000001	10000000	10000001	10000000
A*0101 PIC	15.962	10.624	6.439	5.246	8.786	18.802	9.498	4.161	18.299	19.200	6.117	4.901	8.740	7.960	8.69	4.429	6.022	2.145	3.307	2.218	2.560	1.370	18.149	996.6	18.117	6.934	17.546	16.912
*	0	6	6	6	6	6	0	6	0	6	6	6	01	6	6	6	6	6	6	6	6	6	6	6	6	0	6	6
Sequence	KTNKWEDIY	KSIYIFYTY	<b>GTFTFQNMY</b>	CNDGNILYY	YFECIMKLY	VYEGKLKKY	VVDLFCGVGY	FSSINTYDY	VSNVEDSNY	NSNYNKKLY	KVSDEIWNY	ISGEGLIIY	FVEDSSSFLY	DSDSSNALY	SQDVFILEY	NSMFHIIMY	SSYNLFEEY	SSGKTFICY	ILENILLSY	FSDLILYVY	HIENILLKY	FVEALFQEY	PSDKHIKEY	IMNHLMTLY	LIENELMNY	NVDQQNDMY	SSFFMNRFY	NHEQKLSEY
Peptide No.	98.0038	98.0039	98.0040	98.0041	98.0042	98.0043	1000.86	98.0044	98.0045	98.0046	98.0047	98.0048	98.0002	98.0049	98.0050	98.0051	98.0052	98.0053	98.0054	98.0055	98.0026	98.0057	98.0058	98.0059	98.0060	98.0061	98.0062	98.0063
Position	216	190	986	1298	1379	1389	1650	1770	1803	1831	182	35	215	384	198	1028	1093	1258	1340	1439	2318	4	310	38	149	182	309	342
Accession No.																						CAB38998	CAB38998					
Addn Source info	Chromosome10	Chromosome10	Chromosome10	Chromosome10	Chromosome10	Chromosome10	Chromosome10	Chromosome10	Chromosome10	Chromosome10	Chr12Contig18											MAL3P2.11	MAL3P2.11	Chromosome 11				
Malaria locus	331.100003	331.t00003	331.00003	331.100003	331.00003	331.100003	331.100003	331.100003	331.100003	331.100003	18.000811	MY924Fe3.p1t1	MY924Fe3.p1t1	MY924Fe3.p1t1	MY924Fe3.p1t1	MY924Fe3.plt1	MY924Fe3.p1t1	MY924Fe3.plt1	MY924Fe3.p1t1	MY924Fe3.p1t1	MY924Fe3.plt1	MP03001	MP03001	1369.100001	1369.t00001	1369.t00001	1369.t00001	1369.100001

Table 2: Pf-derived A1 supertype peptides with PIC <20nM

., 02	0.00	0.00	0.00	0.00	0.00	1.9	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	=	£1	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
A*2402 PIC	10000001	1000000.0	1000000	1000000.0	10000000	2826.7	1000000.0	1000000	1000000.0	10000000	10000000	10000000	10000000	1000000	1000000	10000000	1000000	1000000	1043.1	160.3	1000000	1000000.0	1000000	10000000	10000001	1000000	10000000	1000000
A*1101	3608.2	10000000	97274.6	319.3	1000000.0	1357.8	4626.8	52350.4	10000000	22.4	406.1	5.11.7	3889.9	2028.0	630.5	266.9	1646.1	19742.1	2749.2	3766.2	13925.8	5231.6	16168.9	98918.2	209.0	257.7	47876.1	2220.4
A*0201	1000000.0	1000000.0	10000001	10000000	10000000	10000001	10000001	1000000.0	10000000	1000000.0	10000000	10000000	1000000.0	1000000.0	1000000.0	1000000.0	10000000	10000000	10000000	1000000.0	10000000	1000000.0	10000000	10000000	10000000	10000000	10000000	1000000.0
A*0101 PIC	18.838	19.642	19.647	1.491	15.998	806.9	11.791	12.867	13.159	7.495	14.092	6.559	19.553	12.365	1.848	2.466	16.782	7.493	19.854	11.735	1.204	16.821	2.097	7.997	2.825	6.979	5.181	4.783
¥	9	σ	٥	10	6	6	6	6	6	6	6	01	6	01	6	6	6	10	01	6	6	6	6	6	6	6	6	6
Sequence	LSEYYDXDIY	<b>ФЕЕОККУІУ</b>	DSQNELTNY	FSFFFSLIDY	CHEMKAEFY	MFSSIFENY	NSTITTINTA	YIDNDINIY	EEDKTYELY	KTYELYQKY	CTHISYYKY	FVDEEGEQLY	NSLYNKIEY	YSSASESNFY	ASESNFYKY	ASGKLFSLY	GSNKVSDWY	FQDNYLKLDY	<b>FFDYNSQYYY</b>	<b>FFDYNSQYY</b>	MLEQKLSNY	NSFNNSNIY	CSSTKDLNY	YDDDKYNKY	GTYGNMENY	FTYYSCKNY	YDERNTLVY	STDDSKNVY
Peptide No.	98.0003	98.0064	98.0065	98.0004	98.0066	98.0067	98.0068	6900'86	98.0070	98.0071	98.0072	98.0005	98.0073	98.0006	98.0074	98.0075	98.0076	98.0007	98.0008	98.0077	98.0078	98.0079	98.0080	98.0081	98.0082	98.0083	98.0084	98.0085
Position	347	363	313	441	480	548	749	859	919	922	1013	1046	∞	46	49	961	237	511	265	265	669	882	<b>∞</b>	263	638	069	1022	1387
Accession No.																												
Addn Source info	Chromosome 11	Chromosome 11	Chromosome 11	Chromosome 11	Chromosome 11	Chromosome 11	Chromosome 11	Chromosome 11	Chromosome 11	Chromosome 11	Chromosome 11	Chromosome 11																
Malaria locus	1369.100001	1369.t00001	699.100001	699.100001	100001669	699.100001	100001669	100001	100001.669	100001.669	699.100001	100001.669	M13Hg2.q1t3	MI3Hg2.q13	M13Hg2.q1t3	M13Hg2.q1t3	M13Hg2.q1G	M13Hg2.q1t3	M13Hg2.q1t3	M13Hg2.q1t3	M13Hg2.q1t3	M13Hg2.q1t3	Mal_5L10c4.q1t6	Mal_5L10c4.q1t6	Mal_5L10c4.q1t6	Mal_5L10c4.q1t6	Mal_5L10c4.q1t6	Mal_5L10c4.q1t6

Table 2: Pf-derived A1 supertype peptides with PIC <20nM

PIC

A*2402 PIC	100000000	10000000	1000000.0	10000000	10000000	1000000.0	10000001	1000000.0	1000000.0	10000000	10000000	10000001	10000000	10000001	10000000	10000001	10000000	10000000	1000000.0	1000000.0	1000000.0	1000000.0	1000000.0	10000001	1000000.0	10000000	10000001	10000000
A*1101	56737.7	7177.6	19.1	5170.0	93.5	1677.3	6898.3	1804.6	662.3	186.2	318.5	151.7	10960.5	10000001	11938.7	163.8	5804.6	4581.2	30954.5	10000000	4104.6	464.0	10000000	10000000	44.6	544.5	560.9	967.3
A*0201	10000001	1000000.0	10000000	10000000	10000000	1000000.0	10000000	10000001	10000001	10000001	1000000.0	10000000	10000000	1000000.0	1000000.0	1000000.0	10000001	1000000.0	10000000	10000000	1000000.0	10000001	10000001	1000000.0	1000000.0	10000001	10000001	10000000
A*0101 PIC	2.622	6.162	7.670	2.747	2.179	4.189	2.171	5.835	7.282	7.415	6.330	1.127	4.678	2.668	14.664	16.603	13.667	7.537	17.550	18.208	12.836	20.002	10.436	10.234	10.460	15.732	4.229	8.533
\$	6	2	0	6	01	6	6	01	6	6	6	6	٥	01	10	6	0	6	10	6	6	6	6	6	01	6	6	01
Sequence	FSDDNKNLY	YLDNELTINY	STISLNYHY	GLDLKMTLY	YTFQNNNDFY	HTNNKTSIY	FVDPNKYIY	NVEAYHNDNY	YSNNSHAEY	LTNNSSYIY	SSSIYNQNY	GSYGTFLKY	DIDKTVLHY	FNDTQKKGTY	LSASDEYEQY	SASDEYEQY	FQAAESNERY	QAAESNERY	ELEASISGKY	LEASISGKY	NLALLYGEY	SSPLFNNFY	LNEQLIYTY	QNADKNFLY	FVSSIFISFY	VSSIFISFY	YSYYEPLRY	KSNNIIPLLY
Peptide No.	98.0086	6000.86	98.0087	98.0088	98.0010	68.00.86	98.0090	98.0011	98.0091	98.0092	98.0093	98.0094	98.0095	98.0012	98.0013	98.0096	98.0014	98.0097	98.0015	98.0098	98.0099	98.0100	98.0101	98.0102	98.0016	98.0103	98.0104	98.0017
Position	1451	1508	1709	1907	1044	1080	1710	1827	1858	1905	2211	2476	2532	2571	95	96	13	14	81	82	188	14	69	145	255	256	112	250
Accession No.															CAA15614	CAA15614						CAB11150	CAB11150	CAB11150	CAB11150	CAB11150		
Addn Source info					Chromosomel 1	Chromosomel 1	Chromosome11	Chromosomel 1	Chromosome11	Chromosome11	PFC0450w	PFC0450w	Chromosome14	Chromosome14	Chromosome14	Chromosome14	Chromosome14	PFC0700c	PFC0700c	PFC0700c	PFC0700c	PFC0700c	Chromosome14	Chromosome14				
Malaria locus	Mal_5L10c4.q1t6	Mal_5L10c4.q1t6	Mal_5L10c4.q1t6	Mal_5L10c4.q1t6	571.t00003	571.100003	571.t00003	571.t00003	571.100003	571.100003	571.100003	571.t00003	571.t00003	571.100003	MP03072	MP03072	45.t00001	45.t00001	45.t00001	45.100001	45.00001	MP03137	MP03137	MP03137	MP03137	MP03137	12.100018	12.100018

PIC

Table 2: Pf-derived A1 supertype peptides with PIC <20nM

																												•
A*2402 PIC	10000000	1000000.0	10000001	18.3	1000000.0	1000000.0	151.9	100000000	10000000	10000000	1000000.0	10000000	10000001	1000000.0	1000000.0	1208.1	1000000.0	10000000	1000000.0	1000000.0	1000000.0	100000000	1000000.0	1000000.0	1000000.0	1000000.0	10000000	24764.5
A*1101	2243.6	64.6	923.1	10000001	328.7	1330.7	1384.3	774.9	290.6	10000000	10632.6	4191.1	574.3	286.4	1178.7	3568.1	805.6	1.8061	6774.7	3405.9	25.1	24044.7	801.6	635.7	5008.9	1911.2	6184.9	88038.7
A*0201	1000000.0	10000001	10000000	10000000	10000001	10000001	10000000	10000000	10000001	10000001	1000000.0	10000000	10000000	10000001	10000000	10000000	10000001	10000000	10000001	10000000	10000000	10000000	10000001	10000001	10000000	10000000	10000000	10000001
A*0101 PIC	8.006	6.105	6.927	4.639	7.724	0.789	910.9	9.105	3.423	18.436	7.801	4.464	3.940	3.473	4.983	5.609	6.243	15.909	15.648	15.176	10.960	3.907	2.901	4.669	1.423	10.972	5.286	7.244
₹	6	6	6	6	9	6	6	6	6	6	6	01	6	6	6	6	6	10	6	6	6	6	6	6	6	9	0	6
Sequence	SSSDEENLY	SSDEENLYY	KSNWNNNTA	FYDKRFIFY	NVEKNFLLYY	NVEKNFLLY	KMDSFLNVY	NSLIEFLFY	ATYKNGNIY	DEEKIFVKY	HTSNDSGSY	FSFTVGEGKY	ETNNNLFIY	HVSKHAFEY	MSGYSSNNY	<b>FMESAFVNY</b>	RSPCSHKLY	FTGENNIERY	NTLMLKADY	VSSKPANEY	ITYSFTVSY	LVETLDNLY	ETLDNLYLY	LSAKYYISY	HSDIHLLNY	FTSPVNIKEY	YSSYSSPKY	GMERNKTKY
Peptide No.	98.0105	98.0106	98.0107	98.0108	98.0018	98.0109	98.0110	98.0111	98.0112	98.0113	98.0114	98.0019	98.0115	98.0116	98.0117	98.0118	98.0119	98.0020	98.0120	98.0121	98.0122	98.0123	98.0124	98.0125	98.0126	98.0021	98.0127	98.0128
Position	467	468	607	979	969	969	949	1042	80	226	98	136	186	319	387	460	650	629	777	880	27	233	235	295	155	9/9	746	868
Accession No.																												
Addn Source info	Chromosome14																											
Malaria locus	12.00018	12.00018	12.t00018	12.00018	12.100018	12.t00018	12.100018	12.100018	mal_BU121g9.q1c1	mal_9A57b11.q1c2	mal_BL50e8.p1ca_5	mal_BL50e8.plca_5	mal_BL50e8.plca_5	mal_BL50e8.plca_5	mal_BL50e8.plca_5	mal_BL50e8.p1ca_5	mal_BL50e8.p1ca_5	mal_BL50e8.p1ca_5	mal_BL50e8.plca_5	mal_BL50e8.plca_5	M13S8h6.p1t_3	M13S8h6.plt_3	M13S8h6.p1t_3	M13S8h6.p1t_3	M13S8h6.p1t_3	M13S8h6.p1t_3	M13S8h6.p1t_3	M13S8h6.p1t_3

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Table 2: Pf-derived A1 supertype peptides with PIC <20nM

Malaria locus         Addn Source info         Accession         Position         Persiton           413S8h6.p1L_3         1268         98           413S8h6.p1L_3         1268         98           585.100002         Chromosomel1         297         98           585.100002         Chromosomel1         465         98           585.100002         Chromosomel1         465         98           585.100002         Chromosomel1         1021         98           585.100002         Chromosomel1         1161         98           585.100002         Chromosomel1         1739         98           1223.100015         mal_9A21f9.q1t_4         1833         98           1223.100015         mal_9A21f9.q1t_4         165         98           1223.100015         mal_9A21f9.q1t_4         2426         98           1223.100015         mal_9A21f9.q1t_4         4163         98								
1268		de Sequence	¥	A*0101 PIC	A*0201	A*1101	A*2402 PIC	
1488   Chromosome	1268 98.0129	29 YSNIDSGKY	6 *	11.517	1000000.0	14325.6	1000000.0	
Chromosomel I         297           Chromosomel I         465           Chromosomel I         465           Chromosomel I         741           Chromosomel I         1021           Chromosomel I         1161           Chromosomel I         1161           Chromosomel I         1739           mal 9A21f9,q11_4         387           mal 9A21f9,q11_4         1833           mal 9A21f9,q11_4         2426           mal 9A21f9,q11_4         2426           mal 9A21f9,q11_4         2478           mal 9A21f9,q11_4         2476           mal 9A21f9,q11_4         2467           Chromosomel I         26           Chromosomel I         304           Chromosomel I         430           Chromosomel I         430           Chromosomel I         430           Chromosomel I         1018	1488 98.0130	30 LIDLSCIHY	6	3.960	1000000.0	1722.8	10000000	
Chromosome11         381           Chromosome11         465           Chromosome11         741           Chromosome11         741           Chromosome11         1161           Chromosome11         1161           Chromosome11         1739           mal_9A21f9.q1_4         387           mal_9A21f9.q1_4         1853           mal_9A21f9.q1_4         2426           mal_9A21f9.q1_4         2426           mal_9A21f9.q1_4         2426           mal_9A21f9.q1_4         246           mal_9A21f9.q1_4         246           mal_9A21f9.q1_4         246           chromosome11         364           Chromosome11         304           Chromosome11         430           Chromosome11         430           Chromosome11         430           Chromosome11         430	297 98.0131	31 CSDSSLNIY	6 X	2.643	10000000	44436.7	10000001	
Chromosome11         465           Chromosome11         575           Chromosome11         741           Chromosome11         1021           Chromosome11         1161           Chromosome11         1361           Chromosome11         1739           mal_9A21f9,q1t_4         387           mal_9A21f9,q1t_4         165           mal_9A21f9,q1t_4         2426           mal_9A21f9,q1t_4         2426           mal_9A21f9,q1t_4         245           mal_9A21f9,q1t_4         246           mal_9A21f9,q1t_4         246           mal_9A21f9,q1t_4         246           chromosome11         3445           chromosome11         364           Chromosome11         334           Chromosome11         430           Chromosome11         430           Chromosome11         430	381 98.0132	32 VSFDNNENY	6 7	7.080	10000000	824.4	1000000.0	
Chromosomel 1 775  Chromosomel 1 1021  Chromosomel 1 1021  Chromosomel 1 1161  Chromosomel 1 1161  Chromosomel 1 1739  mal_9A21f9.q1t_4 387  mal_9A21f9.q1t_4 1833  mal_9A21f9.q1t_4 24065  mal_9A21f9.q1t_4 24065  mal_9A21f9.q1t_4 24065  mal_9A21f9.q1t_4 2406  mal_9A21f9.q1t_4 24067  Chromosomel 1 26  Chromosomel 1 26  Chromosomel 1 304  Chromosomel 1 304  Chromosomel 1 1018	465 98.0022	22 YTDIINIRY	V 10	1.851	10000000	1716.6	1000000.0	
Chromosomell         741           Chromosomell         1021           Chromosomell         1161           Chromosomell         1319           Chromosomell         1361           Chromosomell         1739           mal_9A21f9,q1t_4         387           mal_9A21f9,q1t_4         1883           mal_9A21f9,q1t_4         2426           mal_9A21f9,q1t_4         2426           mal_9A21f9,q1t_4         2478           mal_9A21f9,q1t_4         2463           chromosomell         26           Chromosomell         304           Chromosomell         430           Chromosomell         430           Chromosomell         6018	575 98.0023	23 LSNIRKPLFY	بل 10	5.132	1000000.0	3669.8	10000000	
Chromosomel 1 1021 Chromosomel 1 1161 Chromosomel 1 1361 Chromosomel 1 1361 Chromosomel 1 1361 Chromosomel 1 1361  mal_9A21f9.q1t_4 387  mal_9A21f9.q1t_4 1583  mal_9A21f9.q1t_4 2406  mal_9A21f9.q1t_4 2426  mal_9A21f9.q1t_4 2478  mal_9A21f9.q1t_4 2478  mal_9A21f9.q1t_4 2478  mal_9A21f9.q1t_4 2476  Chromosomel 1 26  Chromosomel 1 26  Chromosomel 1 304  Chromosomel 1 304  Chromosomel 1 1018	741 98.0133	33 NVDANYCKY	6 73	3.822	1000000.0	813.1	10000001	
Chromosomel 1 1161  Chromosomel 1 1219  Chromosomel 1 1361  Chromosomel 1 1739  mal_9A21f9.q1t_4 387  mal_9A21f9.q1t_4 1583  mal_9A21f9.q1t_4 2309  mal_9A21f9.q1t_4 2406  mal_9A21f9.q1t_4 2426  mal_9A21f9.q1t_4 2406  mal_9A21f9.q1t_4 24067  Chromosomel 1 26  Chromosomel 1 26  Chromosomel 1 304  Chromosomel 1 304  Chromosomel 1 1018	1021 98.0134	34 CVEKNNMSY	6 AS	6.497	10000001	33246.6	10000001	
Chromosomel I 1219  Chromosomel I 1361  Chromosomel I 1739  mal_9A21f9.q1t_4 387  mal_9A21f9.q1t_4 1653  mal_9A21f9.q1t_4 2309  mal_9A21f9.q1t_4 2426  mal_9A21f9.q1t_4 2426  mal_9A21f9.q1t_4 2426  mal_9A21f9.q1t_4 2467  chromosomel I 26  Chromosomel I 304  Chromosomel I 304  Chromosomel I 304  Chromosomel I 183  Chromosomel I 183  Chromosomel I 183	1161 98.0135	35 SSDGKKSEY	6 X	5.530	10000000	8369.5	10000001	
Chromosomel I 1361  Chromosomel I 1739  mal_9A21f9.q1t_4 387  mal_9A21f9.q1t_4 1583  mal_9A21f9.q1t_4 1833  mal_9A21f9.q1t_4 2426  mal_9A21f9.q1t_4 24309  mal_9A21f9.q1t_4 2478  mal_9A21f9.q1t_4 2478  mal_9A21f9.q1t_4 2478  mal_9A21f9.q1t_4 3445  Chromosomel I 26  Chromosomel I 26  Chromosomel I 304  Chromosomel I 304  Chromosomel I 183  Chromosomel I 1018	1219 98.0136	36 RSNNFFFSY	6 Y	6.117	10000000	11.9	1000000.0	
Chromosome11       1739         mal_9A21B.q1t_4       387         mal_9A21B.q1t_4       1583         mal_9A21B.q1t_4       2309         mal_9A21B.q1t_4       2426         mal_9A21B.q1t_4       2478         mal_9A21B.q1t_4       2478         mal_9A21B.q1t_4       2478         mal_9A21B.q1t_4       4163         mal_9A21B.q1t_4       4267         Chromosome11       26         Chromosome11       304         Chromosome11       430         Chromosome11       430         Chromosome11       1018	1361 98.0024	124 FTMVYEKIKY	KY 10	2.669	10000000	726.8	10000001	
mal_9A21f9.q1t_4 387  mal_9A21f9.q1t_4 1065  mal_9A21f9.q1t_4 1583  mal_9A21f9.q1t_4 2309  mal_9A21f9.q1t_4 2426  mal_9A21f9.q1t_4 2426  mal_9A21f9.q1t_4 2478  mal_9A21f9.q1t_4 3445  mal_9A21f9.q1t_4 3463  Chromosomel 1 26  Chromosomel 1 26  Chromosomel 1 304  Chromosomel 1 304  Chromosomel 1 430  Chromosomel 1 1018	1739 98.0137	37 NVDIFLHYY	۶	3.691	1000000	42.6	1000000.0	
mal_9A21f9.q1t_4 1065 mal_9A21f9.q1t_4 1583 mal_9A21f9.q1t_4 1833 mal_9A21f9.q1t_4 2426 mal_9A21f9.q1t_4 2478 mal_9A21f9.q1t_4 2478 mal_9A21f9.q1t_4 2463 mal_9A21f9.q1t_4 2467 Chromosomel 1 26 Chromosomel 1 26 Chromosomel 1 304 Chromosomel 1 183 Chromosomel 1 1018	387 98.0138	38 SSNEIHNFY	4 ک	7.488	1000000.0	19.5	1000000.0	
mal_9A21f9.q1t_4 1583 mal_9A21f9.q1t_4 1833 mal_9A21f9.q1t_4 2426 mal_9A21f9.q1t_4 2478 mal_9A21f9.q1t_4 2778 mal_9A21f9.q1t_4 4163 mal_9A21f9.q1t_4 4267 Chromosomel 1 26 Chromosomel 1 304 Chromosomel 1 183 Chromosomel 1 1018	1065 98.0139	39 GTKLNRTKY	6 X3	6.438	10000000	9805.4	10000001	
mal_9A21f9.q1t_4 1833 mal_9A21f9.q1t_4 2426 mal_9A21f9.q1t_4 2426 mal_9A21f9.q1t_4 2778 mal_9A21f9.q1t_4 4163 mal_9A21f9.q1t_4 4267 Chromosomel 1 26 Chromosomel 1 83 Chromosomel 1 83 Chromosomel 1 183 Chromosomel 1 1018	1583 98.0025	25 ATVSRAGIVY	VY 10	9.716	10000000	351.9	1000000.0	
mal_9A21f9.q1t_4 2426 mal_9A21f9.q1t_4 2426 mal_9A21f9.q1t_4 2778 mal_9A21f9.q1t_4 4163 mal_9A21f9.q1t_4 4267 Chromosome11 26 Chromosome11 183 Chromosome11 304 Chromosome11 304	1833 98.0140	40 YTLSSGTKY	6 Y.	4.847	1000000.0	1878.1	1000000.0	
mal_9A21f9.q1t_4 2426 mal_9A21f9.q1t_4 2778 mal_9A21f9.q1t_4 3445 mal_9A21f9.q1t_4 4163 mal_9A21f9.q1t_4 267 Chromosomel 1 26 Chromosomel 1 183 Chromosomel 1 304 Chromosomel 1 1018	2309 98.0141	41 VSEKEQQLY	۶. و	6.585	1000000.0	56024.7	1000000.0	
mal_9A21f9.q1t_4       2778         mal_9A21f9.q1t_4       3445         mal_9A21f9.q1t_4       4163         mal_9A21f9.q1t_4       4267         Chromosome11       26         Chromosome11       183         Chromosome11       304         Chromosome11       430         Chromosome11       1018	2426 98.0142	42 VVDFERLRY	6 A3	3.185	1000000.0	457.2	10000001	
mal_9A21f9.q1t_4       3445         mal_9A21f9.q1t_4       4163         mal_9A21f9.q1t_4       4267         Chromosomel 1       26         Chromosomel 1       183         Chromosomel 1       304         Chromosomel 1       430         Chromosomel 1       1018	2778 98.0143	43 FIDLYKQMY	6 AJ	5.792	10000001	14889.5	1000000.0	
mal_9A21f9.q1t_4       4163         mal_9A21f9.q1t_4       4267         Chromosome11       26         Chromosome11       183         Chromosome11       304         Chromosome11       430         Chromosome11       1018	3445 98.0144	44 IVDITNVNY	6 <u>⊁</u>	6.389	10000000	1065.1	10000001	
mal_9A21f9.q1t_4       4267         Chromosome11       26         Chromosome11       183         Chromosome11       304         Chromosome11       430         Chromosome11       1018	4163 98.0145	45 LEDVKKILY	9 Y.	9.183	10000000	10000001	1000000.0	
Chromosomel 1         26           Chromosomel 1         183           Chromosomel 1         304           Chromosomel 1         430           Chromosomel 1         1018	4267 98.0146	46 SLDIPDIAY	6 Y	9.566	10000001	1095.4	1000000.0	
Chromosomel 1         183           Chromosomel 1         304           Chromosomel 1         430           Chromosomel 1         1018	26 98.0147	147 SSCQNSLNY	6 73	1.030	10000001	86.7	10000001	
Chromosomel 1 304  Chromosomel 1 430  Chromosomel 1 1018	183 98.0148	48 KSDITNLNY	6 ⊁	4.923	10000000	947.1	1000000.0	
Chromosomel 1 430 Chromosomel 1 1018	304 98.0149	149 ETNNGDLKY	6 73	6.392	10000000	6561.2	1000000.0	
Chromosome11 1018	430 98.0150	150 LSEDNKNRY	6 43	1.171	10000000	178412.8	1000000.0	
	1018 98.0026	26 LLDLRKNGLY	LY 10	3.696	1000000.0	12286.3	1000000.0	
599.t00001 Chromosome11 1412 98	1412 98.0027	27 GVDKSLKIMY	MY 10	8.185	1000000.0	3010.4	1000000.0	

Table 2: Pf-derived A1 supertype peptides with PIC <20nM

A*2402 PIC	1000000.0	10000001	10000000	1000000.0	1000000.0	10000000	1000000.0	10000001	10000000	1000000.0	10000000	10000000	10000000	10000000	10000000	10000000	10000000	1000000.0	1000000.0	10000000	10000000	1000000.0	1000000.0	1000000.0	10000000	1000000.0	1000000.0	10000000
A*1101	73406.9	2007.1	9.177	4003.2	1265.6	2877.4	389.5	249.1	419.1	3255.4	6127.0	4947.2	5019.1	85.1	326.3	793.4	24883.8	1349.4	113941.0	112.4	1911.8	918.8	35096.0	1168.0	18704.2	878.3	40514.9	3464.1
A•0201	1000000.0	0.0000001	10000001	10000000	10000001	1000000.0	10000000	10000001	1000000.0	1000000.0	10000001	1000000.0	1000000.0	1000000.0	10000001	1000000.0	1000000.0	1000000.0	10000001	1000000.0	100000000	1000000.0	10000000	10000001	10000001	1000000.0	10000001	1000000.0
A*0101 PIC	6.553	6.672	9.278	3.444	11.359	6.926	2.697	1.998	15.958	9.314	6.923	3.528	13.157	13.836	8.691	3.979	8.536	2.601	9.348	5.412	5.386	8.064	8.602	9.299	3.352	3.842	10.561	8.449
\$	6	01	6	6	6	6	6	6	0	6	9	6	6	2	6	6	9	9	6	٥	01	01	6	6	6	6	6	6
Sequence	YTPTNKEMY	<b>ESANDSTNYY</b>	<b>LSNSITVSY</b>	GTTQSNNIY	SDDEIIITY	ISSNGKLNY	GSIQNAYLY	GTMRNRKKY	KSLLKNYNY	NVEDTNMLY	NTDNKDVLNY	HTITISQKY	ISQKYTSSY	KTFHRILAVY	KTNGAEERY	GTVPTNLDY	ESSQNSPKNY	QTDFQGWGHY	<b>EADFIKKMY</b>	ATICRAMKY	KTDEQYNENY	YTFKNPPPQY	WLEYFLDDY	ITSSSESEY	YVDIGSNIY	DTCKNIWNY	LSQGKKNTY	NIDCVISPY
Peptide No.	98.0151	98.0028	98.0152	98.0153	98.0154	98.0155	98.0156	98.0157	98.0158	98.0159	98.0029	98.0160	98.0161	98.0030	98.0162	98.0163	98.0031	98.0032	98.0164	98.0165	98.0033	98.0034	98.0166	98.0167	98.0168	98.0169	98.0170	98.0171
Position	1427	1516	1662	1902	27	41	09	381	707	725	1065	1253	1257	1336	228	293	403	639	668	416	1192	1201	1884	2221	45	457	563	928
Accession No.																												
Addn Source info	Chromosome11	Chromosome11	Chromosome11	Chromosome11	M1045c5.p1c.C_6	T28161	T28161	T28161	T28161	128161	T28161	T28161	T28161	T28161	T28161	Chromosome14	Chromosome14	Chromosome14	Chromosome14									
Malaria locus	599.100001	599.100001	599.100001	599.100001	MP01072	MP01072	MP01072	MP01072	. MP01072	MP01072	MP01072	MP01072	MP01072	MP01072	PIR2	PIR2	PIR2	PIR2	PIR2	PIR2	PIR2	PIR2	PIR2	PIR2	55.00004	55.t00004	55.100004	\$5.100004

Table 2: Pf-derived A1 supertype peptides with PIC <20nM

402 C	6464.5	0.000000	0.000000	0.0000001	2720.6	10000000	0.0000001	0.0000001	0.0000001	0.0000001	0.0000001	0.0000001	0.0000001	0.0000001	0.0000001	0.0000001	10000001	0.0000001	45380.9	0.0000001	365.4
A*2402 PIC	84	1000	1000	1000	272	1000	1000	1000	1000	1000	1000	1000	0001	1000	1000	1000	000	1000	453	1000	36
A*1101	413.3	684.9	41445.3	4760.1	21913.6	1846.9	838.9	1000000.0	9.919	1000000.0	20.3	23874.2	2575.9	183727.1	1310.7	75390.5	1000000.0	377275.0	2478.6	368191.0	1000000.0
A*0201	0.0000001	10000001	10000000	10000000	10000000	0.0000001	10000000	10000001	10000001	10000000	10000000	1000000.0	10000000	10000000	10000000	10000000	10000001	1000000.0	1000000.0	10000000	1000000.0
A*0101 PIC	5.144	109.9	3.798	7.735	8.455	12.536	6.590	5.456	6.496	23.541	10.044	10.069	6009	14.646	17.920	8.198	12.047	13.870	3.056	19.772	17.735
*	6	9	6	6	6	10	6	٥	6	6	0	6	6	6	10	6	6	6	6	6	6
Sequence	NMDNLLFTY	FVDHNYNYNY	HSKENQQKY	VSEGYTSTY	<b>FMDSQNGMY</b>	NSANDSFINA	STGINEENY	MNETVFLDY	LTSKVWDTY	KHDALTYMY	LTYMYCVYY	NIDINDLGY	ISSNQFNNY	DIEPLISSY	VTNNDSINNY	<b>ESGKNMEHY</b>	LKDFDMLLY	YIDVEDDDY	DMDDNYYLY	YGDNNKDCY	IYDFNNNSY
Peptide No.	98.0172	98.0035	98.0173	98.0174	98.0175	98.0036	98.0176	98.0177	98.0178	98.0179	98.0180	98.0181	98.0182	98.0183	98.0037	98.0184	98.0185	98.0186	98.0187	98.0188	98.0189
Position	953	1105	1261	1339	1358	1537	27	\$	77	2	14	201	260	400	453	277	898	936	1001	1224	1239
Accession No.																					•
Addn Source info	Chromosome14	Chromosome14	Chromosome14	Chromosome14	Chromosome14	Chromosome14	Chromosome14	Chromosome 14	Chromosome14	Chromosome14	Chromosome14	Chromosomel 1	Chromosome11	Chromosomel 1	Chromosomel 1	Chromosome 11	Chromosomel 1	Chromosome 11	Chromosome 1 l	Chromosomel 1	Chromosomel 1
Malaria locus	55.t00004	55.100004	55.100004	55.100004	55.100004	55.100004	13.t00011	13.00011	13.100011	37.100002	37.100002	674.100001	674,100001	674.t00001	674.t00001	674.100001	674.100001	674.100001	674.100001	674.100001	674.100001

Table 3: Pf-derived A24 supertype peptides with PIC <100nM

Malaria locus	Addn Source info	Accession No. Position Peptide No.	Position	Peptide No.	Sequence	₹	A*0101 PIC	A*0201	A*1101	A*2402 PIC
331.100003	Chromosome10	ì	2	98.0206	FYKKKRNVL	6	67134.0	1000000.0	1000000.0	1.708
331.100003	Chromosome10		011	98.0207	VYEINKNEF	6	84.1	10000000	10000000	2.011
331.100003	Chromosome10		604	98.0208	FFVWGHDMF	6	221.0	10000001	10000000	3.642
331.100003	Chromosome10		684	98.0209	VYNIKENFW	0	123239.4	1000000.0	10000000	2.687
331.100003	Chromosome10		1108	98.0210	KYNLCHNML	6	147073.6	1000000.0	1000000.0	0.324
331.100003	Chromosome10		1268	98.0211	FYVPIKKKL	6	172677.3	1000000.0	10000000	2.705
331.00003	Chromosome10		1365	98.0212	KYEIIGNIL	6	89209.4	1000000.0	10000000	1.961
331.t00003	Chromosome10		1449	98.0213	<b>FWLAIKDIF</b>	6	173.9	1000000.0	10000000	1.093
331.t00003	Chromosome10		1515	98.0214	LYRRRKNLF	6	113.5	10000000	1000000.0	1.220
331.t00003	Chromosome10		1704	98.0215	IYIIKQNSF	6	111.6	10000000	10000000	0.256
18.000811	Chr12Contig18		~	98.0190	LFVCFLIFHF	01	672.3	1000000.0	10000000	19.783
18.00081	Chr12Contig18		<b>∞</b>	1610.86	CFLIFHFFLF	01	1385.7	1000000.0	10000000	18.44
18.000811	Chr12Contig18		•	98.0216	CFLIFHFFL	6	106491.6	10000000	10000000	0.321
18.000811	Chr12Contig18		=	98.0217	IFHFFLFLL	6	53306.2	10000000	10000000	38.527
18.000811	Chr12Contig18		13	98.0192	HFFLFLLYIL	9	10000001	1000000.0	10000000	35.659
18.000811	Chr12Contig18		13	98.0218	HFFLFLLYI	6	24845.8	10000001	10000000	26.159
18.000811	Chr12Contig18		14	98.0219	FFLFLLYIL	6	62569.1	10000000	10000001	32.471
18.000811	Chr12Contig18		61	98.0220	LYILFLVKM	6	90645.8	10000000	10000000	63.051
18.000811	Chr12Contig18		4	98.0221	VFLVFSNVL	6	178682.3	10000000	10000000	5.555
18.000811	Chr12Contig18		160	98.0222	TYGIIVPVL	6	123562.9	10000000	1000000.0	3.015
MY924Fe3.plt1			153	98.0223	FFNVFNIFF	6	45.6	100000000	10000000	0.470
MY924Fe3.p1t1			1412	98.0224	FYSWLQNVL	6	83170.3	10000000	10000000	2.428
MY924Fe3.p1t1			1435	98.0225	FYERFSDLI	6	46149.1	10000001	10000000	0.625
MY924Fe3.p1t1			1534	98.0226	VYLIQNNYI	6	615175.4	10000001	10000000	0.632
MY924Fe3.p1t1			1557	98.0227	NYMKNSFYI	6	24802.7	10000001	1000000.0	2.200
MY924Fe3.plt1			1800	98.0228	VYCNYVTEI	0	160654.7	10000000	10000001	3.071

Table 3: Pf-derived A24 supertype peptides with PIC <100nM

							PIC			
Malaria locus	Addn Source info	Accession No. Position Peptide No.	Position	Peptide No.	Sequence	<b>\{</b>	A*0101 PIC	A*0201	A*1101	A*2402 PIC
MY924Fe3.p1t1			1839	98.0229	HYEVLPYKF	6	14.6	1000000.0	10000000	2.621
MY924Fe3.pltl			1846	98.0230	KFTIIVESL	6	181796.5	10000001	0.0000001	1.946
MY924Fe3.p1t1			2159	98.0231	FMTRAHFHI	6	90206	52.2	10000000	1.455
MY924Fe3.plt1			2380	98.0232	FYKSKVIII	6	53263.7	10000001	1000000.0	0.928
MP03001	MAL3P2.11	CAB38998	=	98.0233	SFLFVEALF	٥	80.3	10000000	1000000.0	53.045
MP03001	MAL3P2.11	CAB38998	54	98.0234	YYGKQENWY	6	73.1	10000001	10000000	49.750
MP03001	MAL3P2.11	CAB38998	369	98.0235	KMEKCSSVF	0	34.0	10000001	10000001	39.989
MP03001	MAL3P2.11	CAB38998	376	98.0236	VFNVVNSSI	6	231723.3	10000001	1000000.0	82.506
1369.t00001	Chromosome 11		34	98.0237	NYMKIMNHL	٥	37582.2	10000000	10000000	4.875
1369.100001	Chromosome 11		225	98.0193	SYKSSKRDKF	01	1632.7	10000001	10000001	46.746
1369.100001	Chromosome 11		264	98.0238	TYKKKNNHI	6	90904.7	10000000	10000001	12.042
1369.100001	Chromosome 11		772	98.0239	<b>AXXNILIVL</b>	6	59837.4	10000000	10000001	11.637
1369.t00001	Chromosome 11		285	98.0240	LYYLFNQHI	6	56431.2	10000001	10000000	5.598
1369.t00001	Chromosome 11		310	98.0241	SFFMNRFYI	6	56480.3	10000001	10000000	80.940
1369.100001	Chromosome 11		316	98.0242	FYITTRYKY	6	45.2	10000001	10000000	3.968
1369.100001	Chromosome 11		328	98.0243	KYINFINFI	6	289163.4	1000000.0	1000000.0	0.095
1369.100001	Chromosome 11		331	98.0244	NFINFIKVL	6	610070.5	10000000	10000001	37.188
1369.100001	Chromosome 11		380	98.0245	KYEALIKLL	٥	105887.8	10000000	10000000	9.605
699.100001	Chromosome 11		443	98.0246	FFFSLIDYF	٥	118.9	1000000.0	1000000.0	1.331
100001.669	Chromosome 11		460	98.0247	KYNIKVCEL	6	98354.1	10000001	10000000	0.429
699.100001	Chromosome 11		487	98.0248	FYLYISFLL	6	34312.8	10000001	10000001	0.417
1000001669	Chromosome 11		664	98.0249	<b>FYTNNANLL</b>	6	42910.8	10000001	1000000.0	0.639
100001.669	Chromosome 11		992	98.0250	EYNPSFFYL	6	22929.4	10000001	10000000	1.772
699.100001	Chromosome 11		845	98.0251	SFIIFKNIF	6	249.9	1000000.0	10000000	3.449
699.00001	Chromosome 11		881	98.0252	LYMNFLKFI	6	34148.2	10000001	1000000.0	4.363
100001669	Chromosome 11		929	98.0253	KYLIILLYI	6	93640.1	10000001	10000001	1.034

Table 3: Pf-derived A24 supertype peptides with PIC <100nM

							PIC			
Malaria locus	Addn Source info	Accession No. Position Peptide No.	Position	Peptide No.	Sequence	*	A*0101 PIC	A*0201	A*1101	A*2402 PIC
699.100001	Chromosome 11		1020	98.0254	KYIYIYIYI	٥	215740.5	1000000.0	10000000	0.296
100001.669	Chromosome 11		1024	98.0255	IYIYIFIYL	6	52331.1	10000000	10000000	2.300
M13Hg2.q1t3			135	98.0256	IYINKLSFF	۵	67.4	1000000.0	1000000.0	3.329
M13Hg2.q1t3			142	98.0257	FFSIKDELF	6	27.2	1000000.0	1000000.0	14.276
M13Hg2.q1t3			156	98.0258	EFLKNNSYF	6	164.9	10000001	1000000.0	20.204
M13Hg2.q13			163	98.0259	YFNIIQQKI	6	45274.1	10000001	1000000.0	13.888
MI3Hg2.q1t3			244	98.0260	WYCSACNFL	6	56993.5	10000001	10000000	7.339
M13Hg2.q1t3			396	98.0261	<b>LYLINNKNL</b>	6	1.108021	0.0000001	1000000.0	28.854
M13Hg2.q1t3			345	98.0262	TYKDANNI	6	71978.1	10000000	10000000	29.035
M13Hg2.q1t3			521	98.0263	VYEKEKQYF	6	103.6	1000000.0	10000000	3.963
M13Hg2.q1t3			553	98.0194	PYFNFFVNYF	10	185.8	1000000.0	10000000	33.503
MI3Hg2.q1t3			886	98.0264	IYNNNNEHI	6	77962.6	1000000.0	10000000	24.919
Mal_SL10c4.q1t6			82	98.0265	EYNKYNEYF	6	90.4	10000000	10000000	3.130
Mal_5L10c4.q1t6			137	98.0266	NYVNNNNVF	6	220.5	1000000.0	10000000	3.441
Mal_5L10c4.q116			321	98.0267	KYPIKYCEL	6	183114.8	10000001	10000000	0.364
Mal_5L10c4.q1t6			416	98.0268	AYHDLIKLF	6	8.99	10000001	0.0000001	4.671
Mal_5L10c4.q1t6			533	98.0269	KYISSVNYF	6	194.8	10000001	10000001	0.018
Mal 5L10c4.q1t6			773	98.0270	KYDWFFNSF	6	34.0	1000000.0	1000000.0	0.374
Mal_5L10c4.q1t6			1183	98.0271	HYVIKKYII	6	133499.1	10000001	10000000	1.507
Mal_5L10c4.q1t6			1259	98.0272	LYLHIHKLF	6	72.0	10000001	10000001	0.343
Mal_5L10c4.q1t6			1323	98.0273	YYRTNYGYI	6	165642.6	1000000.0	10000001	4.072
Mal_5L10c4.q1t6			2054	98.0274	KYLRYHSQL	6	421667.1	10000000	10000001	0.655
571.t00003	Chromosome11		42	98.0275	FYIDKCIHF	6	23.2	1000000.0	10000000	0.120
571.100003	Chromosome11		162	98.0276	FYTNYYQSF	0	48.3	1000000.0	10000001	0.186
571.t00003	Chromosomel 1		177	98.0277	PYINQTNIF	9	228.9	10000000	1000000.0	0.527
571.100003	Chromosome11		807	98.0278	NYPNNANHI	6	176667.0	10000001	10000001	3.103

Table 3: Pf-derived A24 supertype peptides with PIC <100nM

							PIC			
Malaria locus	Addn Source info	Accession No. Position Peptide No.	Position	Peptide No.	Sequence	¥	A*0101 PIC	A*0201	A*1101	A*2402 PIC
571.100003	Chromosome11		834	98.0279	TYNNFHNSY	6	52.4	1000000.0	1000000.0	0.776
571.t00003	Chromosome11		1917	98.0280	YMNNNTYSF	6	7.7	1000000.0	1000000.0	2.132
571.t00003	Chromosome11		2026	98.0281	<b>KYTEGATNF</b>	6	74.8	10000000	10000000	1.964
571.t00003	Chromosome11		2450	98.0282	FYISIIDII	6	150563.0	10000000	1000000.0	1.632
571.100003	Chromosome11		2540	98.0283	YYKEHISEF	6	96.3	1000000.0	100000000	3.143
571.t00003	Chromosome11		2914	98.0284	YYNRANNEI	٥	46291.4	1000000.0	1000000.0	3.342
MP03072	PFC0450w	CAA15614	11	98.0285	AFLLITFLM	6	37258.4	1000000.0	100000000	17.525
MP03072	PFC0450w	CAA15614	53	98.0195	LYVIFLVLLF	91	174.0	0.0000001	1000000.0	185'91
MP03072	PFC0450w	CAA15614	53	98.0286	LYVIFLVLL	6	107336.6	10000000	1000000.0	5.089
MP03072	PFC0450w	CAA15614	98	98.0287	KYVQLASTY	6	65.1	10000001	100000000	70.547
45.t00001	Chromosome14		21	98.0196	RYQDPQNYEL	2	1000000.0	0'0000001	10000000	46.471
45.100001	Chromosome14		40	98.0288	IYYFDGNSW	6	97026.0	10000001	10000000	15.493
45.t00001	Chromosome14		95	98.0289	VYRHCEYIL	6	560574.8	10000000	1000000.0	27.538
45.t00001	Chromosome14		135	98.0290	TWKPTIFLL	6	34068.5	10000001	10000000	26.741
45.100001	Chromosome14		891	98.0291	SYKVNCINF	6	25.3	10000000	100000000	63.592
45.t00001	Chromosome14		216	98.0292	KYNYFIHFF	6	39.1	10000001	10000000	0.380
45.100001	Chromosome14		218	98.0293	NYFIHFFTW	6	95820.5	10000001	10000001	2.156
45.100001	Chromosome14		222	98.0294	HFFTWGTMF	6	17.4	10000001	10000000	6.418
45.t00001	Chromosome 14		229	98.0295	MFVPKYFEL	6	57423.3	10000001	10000000	28.589
45.t00001	Chromosome14		295	98.0296	<b>IYTIIQDQL</b>	6	334935.0	10000000	10000000	9.774
MP03137	PFC0700c	CAB11150	3	98.0197	DFFLKSKFNI	2	10000000	10000001	1000000.0	79.527
MP03137	PFC0700c	CAB11150	4	98.0297	FFLKSKFNI	6	80470.7	10000001	1000000.0	10.043
MP03137	PFC0700c	CAB11150	6	98.0298	KFNILSSPL	6	275819.0	10000000	10000000	48.661
MP03137	PFC0700c	CAB11150	19	98.0299	RMTSLKNEL	6	45471.5	9.6801	1000000.0	50.292
MP03137	PFC0700c	CAB11150	77	98.0300	YYNNENNNY	6	29.9	1000000.0	10000000	2.802
MP03137	PFC0700c	CAB11150	87	98.0301	YYNKSTEKL	6	25069.1	10000001	10000001	6.131

Table 3: Pf-derived A24 supertype peptides with PIC <100nM

Malaria locus	Addn Source info	Accession No. Position Peptide No.	Position	Peptide No.	Sequence	*	A*0101 PIC	A*0201	A*1101	A*2402 PIC
MP03137	PFC0700c	CAB11150	601	98.0302	EYEPTANLL	٥	29899.8	1000000.0	1000000.0	9.359
12.t00018	Chromosome14		479	98.0303	PYEEVENYF	6	118.2	1000000.0	1000000.0	3.525
12.t00018	Chromosome14		909	98.0304	KFILHMTLL	6	418744.3	10000000	1000000.0	7.942
12.00018	Chromosome14		544	98.0305	NFLNIYASL	6	309896.9	10000000	10000001	7.653
12.00018	Chromosome14		594	98.0306	VWKKLIEYF	6	120.2	1000000.0	10000000	7.058
12.t00018	Chromosomel 4		614	98.0307	LYVSMYIPF	6	113.5	1000000.0	1000000.0	6.679
12.t00018	Chromosome14		819	98.0308	MYIPFIKKF	6	62.3	10000001	1000000.0	2.663
12.100018	Chromosome14		625	98.0309	KFYDKRFIF	6	53.3	10000001	1000000.0	1.395
12.100018	Chromosome14		675	98.0310	IYNMYHNNF	6	27.2	0.0000001	0'0000001	0.737
12.00018	Chromosome14		879	98.0311	MYHINNESYF	6	8.19	10000000	1000000.0	5.105
12.100018	Chromosome14		815	98.0312	KYDITKNLI	0,	86746.4	10000000	10000000	2.983
mal BU121g9.q1c1			19	98.0313	GYFKRIFKL	6	39278.5	10000000	1000000.0	64.889
mal_BU121g9.q1c1			8	98.0314	TYKNGNIYI	6	240142.1	100000001	1000000.0	20.110
mal_BU121g9.q1c1			87	98.0315	IYIYIYI	6	133656.3	100000001	10000000	2.246
mal_BU121g9.q1c1			68	98.0198	IYIYIYIYEL	9	1000000.0	10000000	10000000	72.026
mal_BU121g9.q1c1			88	98.0316	IYIYIYIF	6	8.68	10000000	10000000	0.543
mal_9A57b11.q1t2			75	98.0317	IFKNDNNTF	6	290.7	10000000	0.0000001	11.568
mal_9A57b11.q1t2			103	98.0318	KYGNICHHI	6	61693.1	10000000	10000000	4.552
mal_9A57b11.q1t2			139	98.0319	QYTDIPSLI	6	41835.9	10000001	10000001	24.727
mal_9A57b11.q1t2			159	98.0320	VFCYEYFIF	6	98.9	10000000	10000000	69.226
mal_9A57b11.q1t2			191	98.0199	CYEYFIFDIF	9	811.1	10000000	10000000	61.974
mal_9A57b11.q1t2			191	98.0321	CYEYFIFDI	6	32300.1	1000000.0	10000001	79.659
mal_9A57b11.q1t2			171	98.0322	KYARNILSL	6	27927.9	10000001	10000000	3.398
mal_9A57b11.q1t2			230	98.0323	IFVKYLPLF	6	68.2	1000000.0	10000001	30.518
mal_9A57b11.q1t2			233	98.0324	KYLPLFLMM	6	16925.5	10000000	10000001	15.776
mal 9A57b11.q1t2			237	98.0325	LFLMMEHSF	6	51.0	1000000.0	10000001	70.804

Table 3: Pf-derived A24 supertype peptides with PIC <100nM

						1	PIC			
Malaria locus	Addn Source info	Accession No. Position Peptide No.	Position	Peptide No.	Sequence	*	A*0101 PIC	A*0201	A*1101	A*2402 PIC
mal BL50e8.p1ca_5			91	98.0326	QYSNYFDYL	0	103941.7	1000000.0	1000000.0	17.499
mal_BL50e8.p1ca_5			184	98.0327	PYETNNNLF	6	37.2	10000001	1000000.0	4.367
mal_BL50c8.p1ca_5			341	98.0328	YYSRRVEKI	6	33168.4	10000001	0.0000001	6.349
mal_BL50e8.p1ca_5			555	98.0329	KFKWIQDNL	6	453346.6	100000001	10000000	30.007
mal_BL50e8.p1ca_5			289	98.0200	RYVGLGSFHF	01	1143.3	1000000.0	10000001	33.267
mal_BL50e8.p1ca_5			892	98.0330	TYKMYPPEF	6	68.2	100000001	10000000	7.746
mal_BL50e8.pica_5			171	98.0331	MYPPEFNTL	6	37286.8	10000001	10000001	14.291
mal_BL50e8.p1ca_5			827	98.0332	KYCIGSTYF	6	184.3	10000000	10000000	0.261
mal_BL50e8.p1ca_5			833	98.0333	TYFLRQVSI	6	163553.3	10000001	1000000.0	31.623
mal_BL50e8.p1ca_5			857	98.0334	KYSARLHPI	6	52609.1	10000000	10000000	33.171
M13S8h6.plt_3			152	98.0335	FYLKKKFLF	٥	30.5	1000000.0	10000000	0.091
M13S8h6.p1t_3			298	98.0336	KYYISYKVL	0	328554.4	10000001	10000000	3.468
M13S8h6.p1t_3			321	98.0337	KYINKNISL	6	213679.4	10000000	10000000	0.395
M13S8h6.p1t_3			380	98.0338	KYLKEDNTF	6	189.5	1000000.0	10000001	2.580
M13S8h6.p1t_3			753	98.0339	KYGDNENNF	6	50.4	1000000.0	1000000.0	2.048
M13S8h6.p1t_3			1208	98.0340	VFTKINNLF	6	55.7	10000001	1000000.0	4.101
M13S8h6.p1t_3			1438	98.0341	IWLIRSIYL	٥	175087.7	1000000.0	10000000	2.659
M13S8h6.plt_3			14 44	98.0342	IYLFIITYI	9	153399.4	10000000	10000000	4.385
M13S8h6.p1t_3			1536	98.0343	FFFVFFYIF	ò	26.2	1000000.0	10000001	0.631
M13S8h6.p1t_3			1541	98.0344	FYIFLIYSF	6	60.5	10000000	1000000.0	0.315
585.100002	Chromosome11		-	98.0345	MYIFFFILF	6	12.6	100000000	10000001	11611
585.100002	Chromosomel 1		=	98.0346	<b>FYVMSTYTF</b>	6	45.7	10000000	10000001	0.144
\$85.100002	Chromosomel 1		512	98.0347	RYCTKCFLW	6	31357.1	0.0000001	0.0000001	1.726
585.t00002	Chromosomel 1		909	98.0348	VYAKNIPLW	6	36459.4	0.0000001	0.0000001	1.882
585.t00002	Chromosome11		999	98.0349	FFCIFFISL	6	35177.1	0.0000001	0.0000001	1.436
585.100002	Chromosomel 1		189	98.0350	PYYKKKNLF	6	53.3	1000000.0	10000000	2.732

Table 3: Pf-derived A24 supertype peptides with PIC <100nM

Addn Source info Chromosomel 1 S mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 chromosomel 1					PIC			
Chromosomel I Chromosomel I Chromosomel I Chromosomel I Chromosomel I mal_9A21f9.q1t_4 chromosomel I	info Accession No. Position Peptide No.	Peptide No.	Sequence	*	A*0101 PIC	A*0201	A*1101	A*2402 PIC
Chromosome 11  Chromosome 11  Chromosome 11  mal_9A21f9.q1t_4  chromosome 11	lel1 1378	98.0351	FYTLVNILI	0	40959.2	1000000.0	1000000.0	2.113
Chromosomel 1  Chromosomel 1  mal_9A21B.q1t_4  chromosomel 1	le11 1419	98.0352	YFIIRSYEL	6	135598.6	10000001	10000000	2.721
Chromosomel I  mal_9A21f9.q1t_4  chromosomel I	iel1 1483	98.0353	KYICLTCAF	6	30.1	10000001	10000000	0.435
mal_9A21f9.q1t_4 chromosomel 1	iel1 1752	98.0354	KYDLFNNFI	6	83062.5	10000000	10000000	1.355
mal_9A2119.q1t_4 mal_9A2119.q1t_4 mal_9A2119.q1t_4 mal_9A2119.q1t_4 mal_9A2119.q1t_4 mal_9A2119.q1t_4 mal_9A2119.q1t_4 mal_9A2119.q1t_4 mal_9A2119.q1t_4 chromosome11	q1t_4 1202	98.0355	KYKDMAKIF	٥	215.2	10000001	10000000	0.315
mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 Chromosomel I	q1t_4 1599	98.0356	GYRPFIYSW	6	83421.5	1000000.0	10000000	3.292
mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 chromosomel 1	qlt_4 1621	98.0357	LYAIFNKLF	6	57.9	1000000.0	1000000.0	0.212
mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 Chromosomel I	q1t_4 1631	98.0358	FYLDKIQIL	6	36632.3	10000001	10000000	0.942
mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 chromosomel 1	q1t_4 2272	98.0359	RMEDKTFSL	6	8870.6	143.4	10000000	4.349
mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 chromosome11	q1t_4 2702	98.0360	<b>IYNCVTINW</b>	6	10684.6	10000000	0.0000001	2.727
mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 Chromosome11	q1t_4 3109	98.0361	RWTDDSNNF	6	60.4	10000000	10000001	1.600
mal_9A21f9.q1t_4 mal_9A21f9.q1t_4 Chromosomel 1	q1t_4 3735	98.0362	FFYDILNVI	6	40209.1	10000000	10000001	5.095
chromosomel 1	q1t_4 3968	98.0363	KYRKJIYSL	6	215862.1	10000000	0.0000001	0.665
Chromosomel 1	q1t_4 4515	98.0364	KYFIFRIHL	6	114989.5	1000000.0	10000000	0.325
Chromosomel 1	sel1 8	98.0365	KYLTINFFI	6	160943.0	10000000	1000000.0	0.123
Chromosomel 1	tel 1 14	98.0366	FFILLTLVF	6	30.5	10000000	10000001	3.495
Chromosomel 1	iel1 24	98.0367	KYSSCQNSL	6	213208.8	1000000.0	10000001	0.906
Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1 M1045c5.p1c.C_6	iel1 955	98.0368	KFIEHINEF	0	278.8	1000000.0	1000000.0	1.175
Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1 M1045c5.p1c.C_6	1118	98.0369	KYIELNDLI	6	231736.4	10000000	1000000.0	1.464
Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1 M1045c5.p1c.C_6	nel1 1194	98.0370	<b>PYSNVTYVI</b>	6	97127.6	1000000.0	10000000	1.861
Chromosomel 1 Chromosomel 1 Chromosomel 1 M1045c5.p1c.C_6	nel1 1434	98.0371	MYDILNAYF	0	42.0	1000000.0	1000000.0	1.204
Chromosomel 1 Chromosomel 1 M1045c5.p1c.C_6	1769 I 1769	98.0372	HYIMNNTIF	6	38.3	1000000.0	10000000	1.389
Chromosomel 1 M1045c5.p1c.C_6	nel 1 1929	98.0373	FFKYIISYF	6	126.1	1000000.0	10000000	3.000
M1045c5.p1c.C_6	nel 1 1943	98.0374	KYLNDDNYL	6	679247.8	100000001	10000000	0.368
	c.C_6 67	98.0375	LYKSIFKAF	٥	52.5	0.0000001	10000000	21.749
MP01072 M1045c5.plc.C_6	c.C_6 107	98.0376	SYRIVNAGF	9	268.7	10000001	10000000	7.480

Table 3: Pf-derived A24 supertype peptides with PIC <100nM

							PIC		2	ľ
Malaria locus	Addn Source info	Accession No. Position Peptide No.	Position	Peptide No.	Sequence	¥	A*0101 PIC	A*0201	A*1101	A*2402 PIC
MP01072	M1045c5.p1c.C_6		319	98.0377	KYTFRSLSI	6	63496.4	1000000.0	10000000	7.958
MP01072	M1045c5.p1c.C_6		388	98.0378	KYKNDSNRI	6	401700.0	1000000.0	10000001	6.170
MP01072	M1045c5.p1c.C_6		612	98.0379	SYIYNKNIF	6	105.6	1000000.0	10000000	13.043
MP01072	M1045c5.p1c.C_6		1042	98.0380	<b>FMKNNTTLF</b>	6	11.7	10000001	10000001	2.141
MP01072	M1045c5.p1c.C_6		1123	98.0381	HYVMININL	6	52910.4	10000000	10000001	3.607
MP01072	M1045c5.p1c.C_6		1163	98.0382	FFLFFSIFI	6	69264.3	1000000.0	10000000	2.646
MP01072	M1045c5.p1c.C_6	•	1249	98.0383	RYFLHTITI	6	101443.4	1000000.0	10000000	2.834
MP01072	M1045c5.p1c.C_6		1260	98.0384	KYTSSYDSL	6	230897.9	0.0000001	1000000.0	1.533
PIR2	T28161		243	98.0385	YYKLREDWW	6	283854.6	10000000	10000000	8.617
PIR2	T28161		38	98.0386	QYLRWFEEW	6	35188.7	10000000	10000000	14.859
PIR2	128161		628	98.0387	HWTQIKKHF	6	30.8	100000001	10000000	11.497
PIR2	T28161		543	98.0388	HYFVLETVL	6	65432.8	1000000.0	10000000	12.976
PIR2	T28161		833	98.0389	RWMDTAGFI	0	32693.4	1000000.0	10000000	6.822
PIR2	T28161		848	98.0201	IYMPPRRQHF	01	391,2	10000000	1000000.0	14.666
PIR2	T28161		1024	98.0390	RWMTEWAEW	6	39609.0	10000001	10000001	3.877
PIR2	T28161		1574	98.0391	KYQYDKVKL	6	515925.0	1000000.0	10000000	6.877
PIR2	128161		1891	98.0392	KYCRFYKRW	6	239673.9	1000000.0	10000000	3.433
PIR2	T28161		1887	98.0393	YFLDDYNKI	6	114991.6	10000000	1000000.0	7.588
\$5.t00004	Chromosome14		223	98.0394	KYELRKTSI	6	226076.9	10000000	10000000	3.213
55.100004	Chromosome14		339	98.0395	MYKNKVDPL	6	208222.7	10000000	1000000.0	31.490
\$5.00004	Chromosome14		455	98.0396	YYDTCKNIW	6	80910.8	10000000	10000001	11.820
55.100004	Chromosome14		989	98.0397	KYINNMSFI	6	317672.0	1000000.0	10000000	1.757
55.100004	Chromosome14		968	98.0398	LYPWKENKF	6	99.5	10000000	10000001	6.128
55.100004	Chromosome14		973	98.0399	KWNVFNNSI	6	191824.8	1000000.0	1000000.0	0.536
55.100004	Chromosome14		1027	98.0400	KFKIINSYI	6	648818.6	10000000	1000000.0	2.246
55.100004	Chromosome14		1123	98.0401	NYAYDNIEL	6	113781.7	1000000.0	10000000	8.937

Table 3: Pf-derived A24 supertype peptides with PIC <100nM

Malaria locus	Addn Source info	Accession No. Position Peptide No.	Position	Peptide No.	Sequence	\$	A*0101 PIC	A*0201	A*1101	A*2402 PIC
700004 33	Chromosome 14		1155	98.0402	INTSTAIL	6	105468.3	100000000	10000000	7.723
55.10000 <del>04</del>	Chromosome14		1268	98.0403	KYTYNINNL	6	62476.9	1000000.0	10000000	7.681
23.600011	Chromosomel 4		\ %	98.0202	RYNVINHIYL	2	0.0000001	10000000	10000000	74.419
13.00011	Chomosome 4		. <b>%</b>	98.0404	RYNVINHIY	6	26.0	10000000	1000000.0	55.779
13.00011	Chromosome 14		* \$	98.0405	TYNYLTPIL	6	75416.9	10000001	10000000	7.874
13.00011	Chromosome 14		8	98.0203	RFRVFKDYSF	2	3387.1	10000000	10000000	29.344
13.60011	Chromosome 14		8	98.0406	VFKDYSFFI	0	99598.3	10000001	1000000.0	7,373
13.00011	Chromosome14		105	98.0407	FFIDEVKKI	σ	230004.2	10000000	0.0000001	12.686
27 400000	Chromosome14		20	98.0408	VYYDNYESL	٥	72350.5	100000001	10000001	10.652
27.00001	Chromosomell		89	98.0409	RFVEKIYYL	٥	228887.0	1000000.0	10000000	8.045
674.100001	Chromosome11		14	98.0410	IYINVQKNL	6	306183.0	10000001	0.0000001	14.033
674 100001	Chromosomel		140	98.0411	KFYYYFKEF	6	92.8	10000001	10000000	14.487
100000: 42.7	Chromosome1		141	98.0204	FYYYFKEFLL	2	10000001	10000001	10000001	13.628
674 100001	Chromosome11		141	98.0412	FYYYFKEFL	6	104311.6	10000000	10000001	1.300
1000011479	Chromosome 11		418	98.0413	TYIPDKKLL	6	209801.1	10000000	10000001	17.181
674 100001	Chromosome 11		461	98.0414	NYLYNKYYI	0	288938.1	1000000.0	10000000	5.750
200	. Lemocomond		679	98.0415	NFKEOHLLF	o	72.4	10000001	10000000	38.780
6/4.100001	Chromosome11		. £	98.0416	HYINNKHINL	6	41447.1	10000001	10000001	10.887
674.100001	Chromosome 1		0	98.0417	LYREHSREL	0	274526.6	1000000.0	10000000	38.601
100000175	Chromosome! 1		1095	98.0418	NYINNNIYL	6	268777.1	10000000	10000000	3.259
10000	Chromosomer		1117	98.0419	NYNOKENSF	6	40.2	10000000	10000000	27.868
0/4.00001	Cliromosomeru					9	0 /602	0.000001	0 0000001	42 788

Table 4: Pf-derived A2 supertype peptides with PIC <100nM

								PIC		
Malaria locus	Addn Source info	Position	Accessio n No.	Peptide No.	Sequence	¥¥	A*0101	A*0201 PIC	A*1101	A*2402
331.100003	Chromosome10	105		99.0042	LIYPCVYEI	٥	38050.5	43.8	1000000.0	1000000.0
331.t00003	Chromosome10	869		99.0043	NMNVQNFFV	6	50979.5	35.3	10000000	10000000
331.100003	Chromosome10	909		99.0044	FVWGHDMFM	6	25516.6	18.5	10000000	1000000.0
331.t00003	Chromosome10	099		99.0045	QLDDKFAFI	6	3138.5	43.0	1000000.0	1000000.0
331.100003	Chromosome10	950		99.0046	CLINHNFFM	6	63467.3	65.7	1000000.0	1000000.0
331.100003	Chromosome10	957		99.0047	<b>FMLVGGINI</b>	6	11445.4	72.5	100000000	399.0
331.100003	Chromosome10	1001		99.0048	YIIGGGCTV	6	19833.9	6.77	10000000	1000000.0
331.100003	Chromosome 10	1016		99.0049	FTFGSFFDV	6	2705.2	14.1	10000000	1000000.0
331.100003	Chromosome10	1847		99.0050	NLSFAQYTL	6	22775.6	52.7	10000000	1000000.0
331.t00003	Chromosome10	6881		99.0051	RMYHYVVDI	6	47589.4	49.4	100000001	890.2
18.000811	Chr12Contig18	2		1000'66	VLRLFVCFLI	2	10000001	72.4	10000000	1000000.0
18.000811	Chr12Contig18	6		99.0002	FLIFHFFLFL	01	10000001	10.9	1000000.0	1000000.0
18.000811	Chr12Contig18	01		99.0003	LIFHFFLFLL	01	10000001	29.1	1000000.0	1000000.0
18.000811	Chr12Contig18	15		99.0004	FLFLLYILFL	10	404264.4	9.61	10000001	1000000.0
18.000811	Chr12Contig18	32		99.0005	RLPVICSFLV	01	10000000	99.3	10000001	1000000.0
18.000811	Chr12Contig18	35		9000.66	VICSFLVFLV	9	10000001	71.5	10000001	1000000.0
18.000811	Chr12Contig18	39		7000.66	FLVFLVFSNV	2	10000001	45.6	10000001	1000000.0
18.000811	Chr12Contig18	0		99.0052	LIFHFFLFL	6	8592.7	8.6	1000000.0	. 1000000.0
18.000811	Chr12Contig18	17		99.0053	FLLYILFLV	٥	6742.1	1.9	10000000	1000000.0
18.000811	Chr12Contig18	. 35		99.0054	VICSFLVFL	6	43080.6	76.0	1000000.0	1000000.0
18.000811	Chr12Contig18	159		99.0055	ATYGIIVPV	6	18077.0	45.4	10000000	1000000.0
MY924Fe3.plt1		222		8000.66	FLYAFNKYYV	2	538964.2	15.2	1000000.0	10000000
MY924Fe3.plt1		127		99.0026	NMISVVYYI	6	97099.2	14.5	10000001	8.2
MY924Fe3.plt1		299		99.0057	SLCFYFLLL	6	2719.7	20.9	1000000.0	10000000
MY924Fe3.plt1		470		99.0058	ILFLHNYLL	6	31359.3	26.7	1000000.0	1000000.0
MY924Fe3.p1t1		512		99.0059	YLDVYNFLL	0	4353.0	7.2	1000000.0	1000000.0
MY924Fe3.plt1		1209		0900'66	FQLYYMYYL	6	91212.8	4.0	10000000	10000000
MY924Fe3.pltl		1267		1900'66	YVMDKVLRL	6	984.8	45.3	10000001	1000000.0

Table 4: Pf-derived A2 supertype peptides with PIC <100nM

					֡					
Malaria locus	Addn Source info	Position	Accessio n No.	Peptide No.	Sequence	¥	A*0101	A*0201 PIC	A*1101	A*2402
MY924Fe3.p1t1		2260		99.0062	LLFILSHFI	٥	11073.4	23.7	10000000	1000000.0
MY924Fe3.p1t1		2326		99.0063	YLVNYCLVV	6	16842.3	10.9	10000001	10000001
MY924Fe3.plt1		2395		99.0064	KIYVCIYYL	6	157982.7	39.3	1000000.0	1000000.0
MP03001	MAL3P2.11	9	CAB389 98	6000.66	ILSVSSFLFV	2	1000000.0	94.9	1000000.0	1000000.0
MP03001	MAL3P2.11	386	CAB389 98	99.0010	LIMVLSFLFL	9	1000000.0	38.4	1000000.0	1000000.0
MP03001	MAL3P2.11	318	CAB389 98	99.0065	YLNKIQNSL	6	13496.2	78.4	10000000	1000000.0
MP03001	MAL3P2.11	387	CAB389 98	99.0066	IMVLSFLFL	6	8739.3	36.0	1000000.0	2608.6
1369.t00001	Chromosome 11	09		99.0011	VQMMIMIKFM	10	1000000.0	9.96	1000000.0	1000000.0
1369.100001	Chromosome 11	62		99.0012	MMIMIKFMGV	10	10000001	47.1	10000001	1000000.0
1369.t00001	Chromosome 11	6		2900.66	KIYKIIIWI	0	56576.0	72.2	10000001	10000001
1369.100001	Chromosome 11	23		8900'66	YMIKKLLKI	6	4324.7	52.7	10000001	788.9
1369.t00001	Chromosome 11	42		6900'66	LMTLYQIQV	6	32880.1	41.7	10000001	1000000.0
1369.100001	Chromosome 11	89		99.0070	FMGVIYIMI	6	10136.0	616	10000000	58.6
1369.t00001	Chromosome 11	280		1200.66	NILIVLYYL	6	117610.0	42.8	10000000	1000000.0
1369.100001	Chromosome 11	312		99.0072	<b>FMNRFYITT</b>	6	14073.8	47.8	0.0000001	10000000
100001.669	Chromosome 11	488		99.0013	YLYISFLLLI	2	311433.0	34.2	10000000	1000000.0
100001.669	Chromosome 11	1025		99.0014	YIYIFIYLFI	91	10000001	8.61	1000000.0	10000001
100001.669	Chromosome 11	408		99.0073	LLDDYHFET	6	5923.7	39.5	10000000	1000000.0
699.t00001	Chromosome 11	488		99.0074	YLYISFLLL	6	2547.9	11.2	1000000.0	10000001
100001.669	Chromosome 11	572		99.0075	FLTLTVYPI	6	22535.9	28.3	1000000.0	10000000
100001.669	Chromosome 11	159		96.0076	FIIEILELL	6	15575.2	47.0	0.0000001	1000000.0
100001.669	Chromosome 11	782		7200.66	LLYNHITSI	6	62668.0	50.4	10000000	0.0000001
699.100001	Chromosome 11	882		99.0078	YMNFLKFIV	6	14215.9	50.3	1000000.0	1000000.0
699.t00001	Chromosome 11	1033		99.0079	FIYIWLHLI	6	6243.9	15.6	1000000.0	10000000
699.100001	Chromosome 11	1039	,	0800'66	HLIIIFIFV	6	6908.2	11.5	100000000	10000000
M13Hg2.q1t3		576		99.0015	FLMWSSQIII	2	96042.7	91.8	1000000.0	1000000.0
M13Hg2.q1t3		96		99.0081	ILLSRFIFI	6	11278.3	22.9	10000000	1000000.0

Table 4: Pf-derived A2 supertype peptides with PIC <100nM

Addn Source info Position 558 551 558 569 577 723 723 723 724 729 729 729 720 720 720 720 720 720 720 720 721 720 721 720 721 720 720 720 720 720 720 720 720 720 720	Accessio 2 21				A #0201	141101	CUV-#1	
Chromosomel 1	n No. Peptide No.	Sequence	₹	A*0101	PIC	A-1101	A-2402	
Chromosome! I	99.0082	YLNFQDNYL	6	34942.8	9.08	100000001	100000000	
Chromosomel 1	99.0083	NIPYFNFFV	o	86593.7	41.8	1000000.0	10000001	
Chromosome! 1	99.0084	FVNYFEAVV	6	15474.4	100.0	1000000.0	10000000	
Chromosome! 1	99.0085	NIHCYTYFL	0	27934.2	25.6	100000000	10000000	
Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!!	9800'66	FLMWSSQII	6	5275.5	31.9	10000000	10000000	
Chromosomel I	99.0087	LMWSSQIII	0	15320.6	46.4	100000000	614.0	
Chromosome!!  Chromosome!!  Chromosome!!  Chromosome!!  Chromosome!!  Chromosome!!  Chromosome!!  Chromosome!!	8800.66	ILNKISSFV	6	1.16571	6.68	10000000	1000000.0	
Chromosome! I	6800'66	FVFFIIKNV	٥	13366.7	53.5	10000000	1000000.0	
Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!!	0600.66	IQICKLYHV	0	8534.4	35.2	1000000.0	1000000.0	
Chromosome!!  Chromosome!!  Chromosome!!  Chromosome!!  Chromosome!!  Chromosome!!  Chromosome!!	1600.66	YISSVNYFL	6	25585.7	24.2	10000000	1000000.0	
Chromosomel 1	99.0092	YLFQLVQSL	6	4424.1	26.3	10000001	1000000.0	
Chromosome!!  Chromosome!!  Chromosome!!  Chromosome!!  Chromosome!!  Chromosome!!  Chromosome!!	99.0093	SIYFYWFLL	0	13813.9	27.2	10000001	1000000.0	
Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!!	99.0094	YLHIHKLFI	6	46175.4	47.6	1000000.0	1000000.0	
Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!!	99.0095	ILDDSINFV	Q	8148.9	41.5	1000000.0	1000000.0	
Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!!	9600.66	FLPEQSYVL	6	36294.8	55.0	10000001	1000000.0	
Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!!	7600.66	HLVIQIIYV	6	52344.4	36.6	10000001	1000000.0	
Chromosome!!  Chromosome!!  Chromosome!!  Chromosome!!  Chromosome!!  Chromosome!!  Chromosome!!	8600.66	FLSVINASV	6	15607.8	17.1	10000000	0.0000001	
Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!!	9100'66	ILYPSLMPYV	01	1000000.0	81.0	10000000	10000000	
Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1	99.0017	YLFGKVKFYI	01	821413.1	47.5	10000001	1000000	
Chromosome!! Chromosome!! Chromosome!! Chromosome!! Chromosome!!	6600.66	KLINTNFYI	6	109718.5	49.2	10000000	10000001	
Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1	99.0100	KTFIYSNFL	6	34260.6	95.5	10000001	10000001	
Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1	99.0101	SLMPYVECI	6	3307.6	80.4	10000000	10000000	
Chromosome! I Chromosome! I	99.0102	YTNYYQSFI	6	14053.9	63.6	10000001	10000001	
Chromosome! I Chromosome! I	99.0103	FQWEKSNKI	6	17731.1	88.1	1000000.0	10000001	
Chromosome 1	99.0104	FLIKLNNEI	6	32980.5	73.6	10000000	10000001	
Chmmocome 11	99.0105	YMYTNYLNM	٥	5105.1	8.59	10000000	4545.4	
	90106	FQGEYVSNL	6	28240.4	61.4	10000000	1000000.0	
MP03072 PFC0450w 7 CA	CAA156 99.0018	ILILIDAASV	2	1000000.0	88.5	0.0000001	10000000	

Table 4: Pf-derived A2 supertype peptides with PIC <100nM

								PIC		
Malaria locus	Addn Source info	Position	Accessio n No.	Peptide No.	Sequence	¥	A*0101	A*0201 PIC	A*1101	A*2402
MP03072	PFC0450w	61	CAA156 14	6100'66	LLITFLMINL	01	1000000.0	82.3	10000000	1000000.0
MP03072	PFC0450w	46	CAA156 14	99.0020	ALWAIILYV	9	599232.7	38.0	1000000.0	1000000.0
MP03072	PFC0450w	20	CAA156	99.0021	AIILYVIFLV	01	10000001	58.1	1000000.0	1000000.0
MP03072	PFC0450w	22	CAA156 14	99.0022	ILYVIFLVLL	9	1000000.0	33.8	10000001	1000000.0
MP03072	PFC0450w	54	CAA156 14	99.0023	YVIFLVLLFI	9	656413.8	20.3	10000001	10000000
MP03072	PFC0450w	57	CAA156 14	99.0024	FLVLLFIYKA	9	139.6	80.7	498.9	1000000.0
MP03072	PFC0450w	18	CAA156 14	99.0107	FLLITFLMI	٥	5377.9	28.0	1000000.0	1000000.0
MP03072	PFC0450w	47	CAA156 14	8010.66	LVVAIILYV	٥	17753.4	20.8	10000000	10000000
MP03072	PFC0450w	20	CAA156 14	99.0109	AIILYVIFL	٥	35558.1	23.3	1000000.0	1000000.0
MP03072	PFC0450w	51	CAA156 14	99.0110	IILYVIFLV	0	29081.2	23.4	10000001	1000000.0
MP03072	PFC0450w	52	CAA156 14	99.0111	ILYVIFLVL	0	4626.7	49.4	10000000	10000000
MP03072	PFC0450w	\$\$	CAA156 14	99.0112	VIFLVLLFI	6	17063.1	28.6	1000000.0	10000000
45.100001	Chromosome14	22		99.0113	YQDPQNYEL	۵	17446.7	62.2	10000000	1000000.0
45.00001	Chromosome14	134		99.0114	KTWKPTIFL	6	18939.7	87.8	1000000.0	10000001
45.t00001	Chromosome14	142		99.0115	LLNESNIFL	6	13381.3	8.99	1000000.0	1000000.0
45.t00001	Chromosome 14	220		99.0116	FIHFFTWGT	0	54429.1	69.2	100000000	1000000.0
MP03137	PFC0700c	180	CAB111 S0	99.0117	VLFLQMMNV	6	71815.8	72.3	10000001	10000000
MP03137	PFC0700c	251	CAB111 50	99.0118	NQMIFVSSI	6	39082.0	99.1	10000000	1000000.0
MP03137	PFC0700c	253	CAB111 50	99.0119	MIFVSSIFI	6	17820.1	95.9	1000000.0	1000000.0
MP03137	PFC0700c	258	CAB111 50	99.0120	SIFISFYLI	6	13357.1	72.3	0.0000001	1000000.0
MP03137	PFC0700c	293	CAB111 50	99.0121	RLFEESLGI	6	22704.6	90.4	10000000	10000000
12.t00018	Chromosome14	870		99.0025	YLCLYNGLLL	2	294216.7	1.62	10000000	1000000.0
12.t00018	Chromosome14	1018		99.0026	YLLFFREKFL	2	10000000	87.8	1000000.0	1000000.0

Table 4: Pf-derived A2 supertype peptides with PIC <100nM

Malaria locus	Addn Source info	Position	Accessio n No.	Peptide No.	Sequence	<b>\{</b>	A*0101	A*0201 PIC	A*1101	A*2402
12.t00018	Chromosome14	597		99.0122	KLIEYFLNM	٥	8556.1	30.0	10000000	1000000.0
12.t00018	Chromosome14	615		99.0123	YVSMYIPFI	6	7.7967.7	57.9	1000000.0	10000000
12.t00018	Chromosome14	870		99.0124	YLCLYNGLL	6	12899.1	8.89	1000000.0	1000000.0
12.t00018	Chromosome14	893		99.0125	NIISSIFYI	6	94922.9	77.9	10000000	10000000
12.100018	Chromosome14	200		99.0126	YLYDNYSHL	6	11094.9	55.2	1000000.0	10000000
12.100018	Chromosome14	953		99.0127	FLNVYENFL	6	23398.0	34.3	10000000	1000000.0
12.t00018	Chromosome14	1037		99.0128	LIFGYNSLI	٥	26493.2	50.1	1000000.0	1000000.0
12.t00018	Chromosome14	1047		99.0129	FLFYGCREV	6	24096.2	30.4	10000000	1000000.0
mal_BU121g9.q1c1		06		99.0130	YIYIYIYEL	6	32096.6	3.8	100000001	1000000.0
mal_BU121g9.q1c1		92		99.0131	YIYIYELQI	6	15022.6	13.6	10000000	1000000.0
mal_9A57b11.q1t2		138		99.0132	KQYTDIPSL	٥	184531.0	81.9	10000000	1000000.0
mal_9A57b11.q1t2		158		99.0133	KVFCYEYFI	6	10650.1	18.0	1000000.0	10000001
mal_9A57b11.q1t2		165		99.0134	FIFDIFKYA	6	21.1	20.2	44.0	100000000
mal_BL50e8.p1ca_5		9		7200.66	ALLSFLVVLV	2	10000001	42.5	10000000	10000000
mal_BL50c8.p1ca_5		9		99.0028	RQINFMETFV	0	10000001	54.6	10000000	10000001
mal_BL50e8.plca_5		4		99.0135	FVALLSFLV	6	3130.0	26.0	1000000.0	1000000.0
mal_BL50e8.plca_5		7		99.0136	LLSFLVVLV	6	11579.5	36.2	1000000.0	1000000.0
mal_BL50e8.p1ca_5		192		99.0137	FIYNWVLQT	6	30528.1	55.9	1000000.0	1000000.0
mal_BL50e8.p1ca_5		349		99.0138	ILIRALLSL	6	8963.2	44.4	1000000.0	10000001
mal_BL50e8.p1ca_5		353		99.0139	ALLSLDFSL	6	22110.4	36.6	10000000	1000000.0
mal_BL50e8.plca_5		295		99.0140	NLFGGGFYI	6	22065.3	23.4	1000000.0	1000000.0
mal_BL50e8.p1ca_5		779		99.0141	LMLKADYFI	6	22456.0	21.9	0.0000001	444.0
mal_BL50e8.p1ca_5		973		99.0142	NIYTHSVYV	φ	245555.5	53.7	10000000	1000000.0
M13S8h6.p1t_3		7		99.0143	FVLACVLLI	6	10293.7	14.2	10000000	1000000.0
M13S8h6.p1t_3		23		99.0144	ATSTFFFFL	0	3703.8	20.0	1000000.0	1000000.0
M13S8h6.p1t_3		*		99.0145	FLLICGFCI	6	23058.3	21.3	1000000.0	10000001
M13S8h6.plt_3		55		99.0146	VLITYSFTV	6	35516.3	7.8	1000000.0	10000001
MI3S8h6 nlt 3		19		99 0147	FTVSVIFFM	6	18627.5	0.0	1000000	1000000

Table 4: Pf-derived A2 supertype peptides with PIC <100nM

								FIE		-
Malaria focus	Addn Source info	Position	Accessio n No.	Peptide No.	Sequence	\$	A*0101	A*0201 PIC	A*1101	A*2402
M13S8h6.p1t_3	3	11		99.0148	LLVCISILL	٥	4378.4	24.2	1000000.0	1000000.0
M13S8h6.p1t_3		1447		99.0149	FIITYIWII	6	50315.1	20.9	10000000	1000000.0
M13S8h6.p1t 3		1469		99.0150	KMMWTIFIL	6	13621.2	14.7	10000000	35.6
M13S8h6.plt 3		1538		99.0151	FVFFYIFLI	6	2681.7	3.2	10000001	1000000.0
M13S8h6.p1t_3		1582		99.0152	YLDRIQFLV	6	3212.4	0.9	1000000.0	1000000.0
585.t00002	Chromosomel I	159		99.0029	VLSPFSLIFV	2	236320.1	33.8	100000000	10000000
585.t00002	Chromosomel 1	1380		99.0030	TLVNILILFL	01	10000000	25.5	10000001	10000001
585.100002	Chromosome11	1406		99.0031	FVFFRFLFFV	01	132657.2	16.7	10000001	10000001
585.100002	Chromosome11	9		99.0153	FILFYFYVM	6	18702.2	8.91	1000000.0	10000001
585.100002	Chromosome11	11		99.0154	YTFCFLPVL	6	3159.4	24.6	10000000	10000000
585.t00002	Chromosome11	643		99.0155	WLFFFDLVV	6	13858.2	39.1	10000001	1000000.0
585.100002	Chromosome11	199		99.0156	HLFFCIFFI	6	13336.6	6.4	1000000	1000000.0
585.100002	Chromosome 11	1386		99.0157	ILFLICYSI	6	18185.7	17.8	1000000.0	10000001
585.100002	Chromosome 11	1399		99.0158	YMFSYIPFV	6	20964.1	<b>:</b> :	10000001	1000000
585.t00002	Chromosomel 1	1507		99.0159	YILFILFFI	6	12765.9	4.2	10000001	10000000
1223.t00015	mal_9A21f9.q1t_4	1387		99.0032	LIHDDVLLFL	2	10000000	32.2	1000000.0	10000000
1223.t00015	mal_9A21f9.q1t_4	270		99.0160	FVSFYKFEV	6	10792.4	28.2	10000001	10000001
1223.r00015	mal_9A21f9.q1t_4	811		99.0161	MLWCSMESV	6	5755.3	27.5	1000000.0	10000001
1223.t00015	mal_9A21f9.q1t_4	924		99.0162	KLFDAINYL	0	35603.1	20.5	1000000.0	1000000.0
1223.t00015	mal_9A21f9.q1t_4	1648		99.0163	FVMDITDSI	6	4215.8	44.1	10000001	10000000
1223.t00015	mal_9A21f9.q1t_4	1853		99.0164	MLYSIVWGL	6	18338.7	24.8	10000001	1000000.0
1223.00015	mal_9A21f9.q1t_4	2301		99.0165	NIYFSYFYV	6	68948.8	41.1	0.0000001	1000000.0
1223.100015	mal_9A21f9.q1t_4	2548		99:0166	FILEHVNSI	6	80628.8	42.2	10000001	10000000
1223.100015	mal_9A21f9.q1t_4	3057		99.0167	SLLKAQLFV	6	12372.4	15.7	10000000	10000000
1223.00015	mal_9A21f9.q1t_4	4419		89.0168	SLDEVVLYT	6	8137.8	46.3	10000000	1000000.0
599.t00001	Chromosome11	6901		99.0033	HLMHIINVFI	2	10000001	86.9	1000000.0	10000000
100001.665	Chromosomel 1	1341		99.0034	FLSDYTTCSV	2	93945.4	72.2	1000000.0	10000000
599.100001	Chromosome11	1458		99.0035	FLRNYVVIFI	2	615882.5	83.6	10000001	1000000.0

Table 4: Pf-derived A2 supertype peptides with PIC <100nM

Malaria locus	Addn Source info	Position	Accessio n No.	Peptide No.	Sequence	*	A*0101	A*0201 PIC	A*1101	A*2402
599.100001	Chromosome11	6		6910'66	YLTINFFIL	6	4373.8	64.1	1000000.0	1000000.0
599.t00001	Chromosome11	883		99.0170	NMNDIENFV	6	32886.3	78.0	1000000.0	0.0000001
599.t00001	Chromosomel 1	1013		1710.66	FIHDILLDL	6	11903.4	46.8	10000001	10000001
599.100001	Chromosomel 1	1034		2210.66	NQYAYDLKI	0	38604.8	81.2	10000000	10000001
599.100001	Chromosome 11	1718		99.0173	GLGGLLFII	6	5216.8	74.2	10000001	1000000.0
599.100001	Chromosome11	1770		99.0174	YIMNNTIFT	0	4444.5	75.2	10000001	10000000
599.t00001	Chromosome11	1914		99.0175	HLFNFSNFV	6	16629.7	25.5	10000001	10000000
MP01072	M1045c5.p1c.C_6	1138		99.0036	YLIRNILMSI	2	819635.3	75.5	1000000.0	10000000
MP01072	M1045c5.p1c.C_6	99		96.0176	YLYKSIFKA	6	6.2	29.5	1755.3	10000000
MP01072	M1045c5.p1c.C_6	82		7110.66	YLDFYEFCV	6	5138.7	6.7	10000000	1000000.0
MP01072	M1045c5.p1c.C_6	1161		99.0178	KIFFLFFSI	6	19713.1	7.22	10000000	10000000
MP01072	M1045c5.p1c.C_6	1281		99.0179	KLNEINILL	6	15599.8	69.4	1000000.0	10000000
PIR2	T28161	577		99.0037	FLMFWVAHM L	2	60152.9	33.4	1000000.0	1000000.0
PIR2	T28161	142		99.0180	LLAEVCYAA	6	8.6	35.1	4774.0	1000000.0
PIR2	T28161	369		99.0181	CLYVCDPYV	6	78244.5	58.0	1000000.0	10000001
PIR2	T28161	577		99.0182	FLMFWVAHM	0	3061.0	5.7	10000001	1000000.0
PIR2	T28161	642		99.0183	FQGWGHYFV	6	53546.0	13.8	1000000.0	10000000
PIR2	T28161	888		99.0184	FLGDVLFAA	6	6.7	8.3	2549.7	10000000
PIR2	T28161	892		99.0185	VLFAANYEA	6	25.8	20.9	100.0	1000000.0
PIR2	T28161	1098		98.0186	YLQAQTTAA	6	26.9	64.0	17290.2	1000000.0
PIR2	T28161	1461		2810'66	FLRQMFYTL	6	8.6228	8.09	1000000.0	1000000.0
PIR2	T28161	2149		99.0188	FAAFTYFYL	o	11639.0	. 45.5	10000000	1000000.0
55.100004	Chromosome14	1358		99.0038	FMDSQNGMYI	2	26503.4	87.2	1000000.0	4109.6
55.00004	Chromosome14	1542		99.0039	SLINYNKYFV	01	10000000	43.5	10000001	1000000.0
55.t00004	Chromosome14	84		99.0189	FVVAQLYEL	6	27995.5	19.7	1000000.0	1000000.0
55.t00004	Chromosome14	480		99.0190	KTFFFFSNV	0	10931.8	72.4	10000000	10000000
55.t00004	Chromosome14	1098		1610.66	IINSDDYFV	6	58940.8	86.9	1000000.0	10000000
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Table 4: Pf-derived A2 supertype peptides with PIC <100nM

								PIC		
Malaria locus	Addn Source info	Position	Accessio n No.	Accessio Peptide No. n No.	Sequence	₩	A*0101	A*0201 PIC	A*1101	A*2402
674.100001	Chromosome11	68	i i	99.0040	ELVEFIFLLL	2	10000000	97.4	10000000	10000001
674.t00001	Chromosome11	281		99.0041	FLYKDVLMDI	01	358012.1	50.4	1000000.0	0.0000001
674.100001	Chromosome 11	88		99.0193	ELVEFIFLL	6	21772.0	47.1	10000000	1000000.0
674.100001	Chromosome11	1102		99.0194	YLNKANPNI	0	12319.8	91.3	10000000	10000000
674.100001	Chromosome11	1353		99.0195	FLQYRIPHM	6	33178.8	81.0	10000000	0.0000001
674.100001	Chromosome11	1430		99.0196	YIVDIFCKI	6	11720.4	48.5	10000000	1000000.0

Table 5: Pf-derived A3,11 supertype peptides scoring positive on PIC algorithm

Malaria locus	Addn Source info	Position	Accession No.	Peptide No.	Sequence	¥¥	A*0101	A*0201 PIC	A*1101 PIC	A*2402
331.100003	Chromosome10	354		7610.66	KFEPFIIHVK	2	1000000.0	10000000	26.5	1000000.0
331.100003	Chromosome10	5		99.0294	KTMDTFYKK	6	2654.1	1000000.0	0.4	1000000.0
331.100003	Chromosome10	208		99.0295	SFFDVSKKK	6	130857.6	1000000.0	16.4	1000000.0
331.100003	Chromosome10	435		99.0596	LSQLVHFYK	6	29656.2	10000001	9.0	1000000.0
331.100003	Chromosome10	779		99.0297	SVFVRRYIK	6	0.16681	1000000.0	0.7	10000000
331.100003	Chromosome10	886		99.0298	FTFQNMYVR	6	5834.2	1000000.0	22.0	1000000.0
331.t00003	Chromosome10	1324		99.0299	SQNSNTFLK	6	10099.5	1000000.0	0.4	10000000
331.100003	Chromosome10	1337		99.0300	ILFHKFLNK	6	3064.6	10000000	2.4	10000000
331.100003	Chromosome10	1521		99.0301	NLFDENFCR	6	30418.9	1000000.0	165.9	1000000.0
331.100003	Chromosome10	1551		99.0302	ALYEKVHGK	6	9346.6	10000000	4.4	1000000.0
18.000811	Chr12Contig18	17		8610.66	FLLYILFLVK	2	10000001	100000000	82.1	10000000
18.000811	Chr12Contig18	43		99.0199	LVFSNVLCFR	01	365585.5	10000000	14.5	1000000.0
18.000811	Chr12Contig18	80		99.0200	<b>AFLESQSMNK</b>	0	10000001	10000000	65.8	1000000.0
18.000811	Chr12Contig18	112		99.0201	TFLESSFDIK	01	1000000.0	10000001	323.9	1000000.0
18.00081	Chr12Contig18	116		99.0202	SSFDIKSEVK	10	10000001	1000000.0	34.1	1000000.0
18.000811	Chr12Contig18	8		99.0303	LLYILFLVK	6	5498.6	10000001	10.1	1000000.0
18.000811	Chr12Contig18	129		99.0304	KSMLKELIK	6	5942.8	10000001	12.7	1000000.0
18.000811	Chr12Contig18	166		99.0305	PVLTSLFNK	6	10202.9	10000000	10.1	10000000
MY924Fe3.plt1		1262		99.0203	TFICYYVMDK	2	10000000	10000000	23.0	0.0000001
MY924Fe3.plt1		155		99:0306	NVFNIFFEK	6	10371.8	10000001	0.2	1000000.0
MY924Fe3.p1t1		220		99.0307	SSFLYAFNK	6	12434.3	10000001	0.1	1000000.0
MY924Fe3.p1t1		1030		99.0308	MFHIIMYTK	6	208352.1	1000000.0	18.2	10000000
MY924Fe3.p1t1		1811		99.0309	SLDDIYKYK	6	22644.9	10000001	2.9	1000000.0
MY924Fe3.p1t1		1613		99.0310	KVVVKNLYK	6	34654.1	10000001	6.0	1000000.0
MY924Fe3.p1t1		1853		99.0311	SLFRLGFVK	6	10283.0	10000001	0.2	10000000
MY924Fe3.p1t1		2012		99.0312	SLFFNSLYY	6	4.6	10000001	5.6	1000000.0
MANOTAEs - 141		9,00				•		0 00000		

Table 5: Pf-derived A3,11 supertype peptides scoring positive on PIC algorithm

Malaria locus	Addn Source info	Position	Accession No.	Peptide No.	Sequence	₹	A*0101	A*0201 PIC	A*1101 PIC	A*2402
MY924Fe3.p1t1		2285		99.0314	SQYEENKSK	6	139775.3	1000000.0	39.1	10000000
MP03001	MAL3P2.11	57	CAB38998	99.0204	KQENWYSLKK	10	10000000	10000000	9.09	10000000
MP03001	MAL3P2.11	335	CAB38998	99.0205	VTCGNGIQVR	10	1000000.0	1000000.0	170.6	1000000.0
MP03001	MAL3P2.11	17	CAB38998	99.0315	ALFQEYQCY	6	3.4	10000001	72.7	1000000.0
MP03001	MAL3P2.11	57	CAB38998	99.0316	KQENWYSLK	6	44996.2	10000000	173.7	1000000.0
1369.t00001	Chromosome 11	44		99.0206	TLYQIQVMKR	≗	100000000	10000001	52.0	1000000.0
1369.t00001	Chromosome 11	28		99.0207	KQVQMMIMIK	9	1000000.0	10000000	8.7	1000000.0
1369.t00001	Chromosome 11	02		99.0208	GVIYIMIISK	91	10000000	10000000	10.6	1000000.0
1369.100001	Chromosome 11	158		99.0209	ELFDKDTFFK	2	1000000.0	0.0000001	14.2	1000000.0
1369.t00001	Chromosome 11	18		99.0317	KTMNNYMIK	6	16730.1	1000000.0	==	1000000.0
1369.t00001	Chromosome 11	159		99.0318	LFDKDTFFK	6	32977.1	1000000.0	126.3	10000001
1369.t00001	Chromosome 11	287		99.0319	YLFNQHIKK	6	21347.4	1000000.0	8.2	1000000.0
1369.t00001	Chromosome 11	307		99.0320	MQSSFFMNR	6	12685.3	1000000.0	25.4	10000001
1369.100001	Chromosome 11	315		99.0321	RFYITTRYK	6	258367.4	1000000.0	21.4	1000000.0
1369.t00001	Chromosome 11	319		99.0322	TTRYKYLNK	6	10429.2	1000000.0	4.5	10000000
100001.669	Chromosome 11	464		99.0210	KVCELLGYYK	2	10000000	10000000	1.1	10000001
699.t00001	Chromosome 11	492		99.0211	SFLLLIVFSK	2	10000001	1000000.0	21.9	1000000.0
699,100001	Chromosome 11	623		99.0212	KLLYKMNYLK	01	10000001	10000001	15.0	10000001
699.100001	Chromosome 11	764		99.0213	TLEYNPSFFY	2	91.9	10000000	219.0	10000001
1000001	Chromosome 11	782		99.0214	LLYNHITSIK	9	10000001	10000001	12.1	10000001
699.100001	Chromosome 11	878		99.0215	LFYLYMNFLK	9	1000000.0	10000001	8.2	1000000
. 699.100001	Chromosome 11	386		99.0323	KQNIPIYIY	o	87.8	10000001	175.4	1000000
699.100001	Chromosome 11	507		99.0324	KTNIFFKKK	6	23058.6	10000001	1.5	1000000.0
1000001669	Chromosome 11	734		99.0325	IVNDLGIFY	6	2.4	100000001	9.91	10000000
100001669	Chromosome 11	769		99.0326	<b>PSFFYLSFK</b>	6	22074.6	1000000.0	20.1	10000000
mal_4T2c4.plt1		15		99.0216	ILLIRPMLVK	2	1000000.0	10000000	95.1	1000000.0
mal 4T2c4.plt1		53		99.0217	LVKLRPMLVK	91	10000001	10000001	22.3	1000000.0

Table 5: Pf-derived A3,11 supertype peptides scoring positive on PIC algorithm

Addn Source info Po  11  11  12  3  3  14  16  16  16  16  16  16  Chromosomel 1  Chromosomel 1									2		
Chromosome11 Chromosome11 Chromosome11 Chromosome11	aria locus	Addn Source info	Position	Accession No.	Peptide No.	Sequence	*	A*0101	A*0201 PIC	A*1101 PIC	A*2402
Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1	4T2c4.plt1		36		99.0218	LVKLGPILVK	2	100000000	1000000.0	15.0	1000000.0
Chromosome11 Chromosome11 Chromosome11 Chromosome11	4T2c4.p1t1		91		99.0327	LLIRPMLVK	6	29115.0	0.0000001	16.1	10000001
Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1	3Hg2.q1t3		97		99.0219	LLSRFIFIYK	2	10000000	10000000	12.9	10000000
Chromosome11 Chromosome11 Chromosome11 Chromosome11	3Hg2.q13		267		99.0220	KTSDAKLVDK	2	543207.5	10000001	21.8	10000001
Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1	3Hg2.q1t3		777		99.0221	ETSTISTFIK	10	714638.7	10000001	21.8	10000001
Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1	3Hg2.q1t3		406		99.0222	<b>IFFSYNPFHK</b>	2	0.0000001	10000001	18.5	1000000.0
Chromosomel I Chromosomel I Chromosomel I Chromosomel I	3Hg2.q1t3		528		99.0223	YFFNCIQMAK	2	1000000.0	10000001	48.6	10000000
Chromosomel I Chromosomel I Chromosomel I Chromosomel I	3Hg2.q13		6		99.0328	SLYNKJEYR	6	32837.9	10000000	36.8	10000001
Chromosomel 1 Chromosomel 1 Chromosomel 1	3Hg2.q1t3		48		99.0329	SASESNFYK	0	17208.3	10000001	0.2	10000001
Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1	3Hg2.q1t3		216		99.0330	ISYIFPLFK	6	12671.6	10000001	2.2	10000000
Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1	3Hg2.q1t3		420		99.0331	SQNYENINK	6	36248.0	10000001	3.6	10000001
Chromosomel I Chromosomel I Chromosomel I Chromosomel I	3Hg2.q1t3		199		99.0332	SLMDASKNK	6	5327.4	10000001	3.2	1000000.0
Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1	5L10c4.q1t6		21		99.0333	KLGFFVCYK	6	42997.2	1000000.0	3.5	10000000
Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1	SL10c4.q1t6		36		99.0334	SFKNKILQK	6	139254.7	1000000.0	14.9	1000000.0
Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1	SL10c4.q1t6		99		99.0335	KFMYLRKKK	6	74875.0	10000000	33.4	10000000
Chromosomel 1 Chromosomel 1 Chromosomel 1	SL10c4.q1t6		381	•	99.0336	KQIIFEALK	6	120283.5	1000000.0	38.9	10000000
Chromosomel I Chromosomel I Chromosomel I Chromosomel I	SL10c4.q1t6		519		99.0337	ETFYKELYK	6	14646.9	1000000.0	1.2	1000000.0
Chromosomel 1 Chromosomel 1 Chromosomel 1	5L10c4.q1t6		537		99.0338	SVNYFLLER	0	4574.8	10000000	0.4	1000000.0
Chromosomel I Chromosomel I Chromosomel I Chromosomel I	5L10c4.q1t6		724		99.0339	ILNFLNFNK	0	12039.7	1000000.0	2.7	10000000
Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1	5L10c4.q1t6		897		99.0340	NTCSKEIYK	0	26259.6	10000000	4.6	1000000.0
Chromosomel I Chromosomel I Chromosomel I Chromosomel I	SL10c4.q1t6		1316		99.0341	KLRNFLFYY	6	34.8	10000000	27.7	10000000
Chromosomel 1 Chromosomel 1 Chromosomel 1 Chromosomel 1	5L10c4.q1t6		1722		99.0342	CSNNNIFYK	6	16887.2	10000000	2.7	1000000.0
Chromosomel I Chromosomel I Chromosomel I	71.00003	Chromosome11	1059		99.0224	MQYNHDNIYK	10	1000000.0	0.0000001	8.9	1000000.0
Chromosomel 1 Chromosomel 1	71.100003	Chromosome! I	2438		99.0225	SFSMLYLFGK	91	1000000.0	1000000.0	20.1	10000000
Chromosomel 1	71.100003	Chromosome11	675		99.0343	ALNPKYQNH	6	4302.1	10000000	149.6	1000000.0
;	71.t00003	Chromosomel 1	749		99.0344	TLNSFQHNK	6	9140.5	10000001	4.0	10000000
Chromosome11	571.100003	Chromosome11	1220		99.0345	KINEFQWEK	6	\$5899.8	10000000	0.3	10000000

Pf-derived A3,11 supertype peptides scoring positive on PIC algorithm

Malaria locus	Addn Source info	Position	Accession No.	Peptide No.	Sequence	¥	A*0101	A*0201 PIC	A*1101 PIC	A*2402
571.t00003	Chromosomel 1	1368		99.0346	RSDYFHNTK	6	15625.8	1000000.0	5.2	1000000.0
571.t00003	Chromosomel 1	1429		99.0347	STNSQQLIK	0	14992.1	10000001	Ξ	10000001
571.100003	Chromosomel 1	1552		99.0348	KFMTPTTLK	6	54389.6	1000000.0	8.1	10000001
571.100003	Chromosome11	1684		99.0349	TTNSTPHFK	0	83088	1000000.0	3.8	10000000
571.t00003	Chromosome11	2509		99.0350	KLMETRFSK	0	8313.3	1000000.0	2.8	10000000
MP03072	PFC0450w	36	CAA15614	99.0226	SQAHRENGKK	≘	100000001	10000000	109.2	1000000.0
MP03072	PFC0450w	45	CAA15614	99.0227	KALVVAIILY	0	220.1	1000000.0	237.1	10000001
MP03072	PFC0450w	55	CAA15614	99.0228	VIFLVLLFIY	10	137.2	10000001	8.19	10000001
MP03072	PFC0450w	99	CAA15614	99.0229	IFLVLLFIYK	01	1000000.0	10000001	44.3	10000001
MP03072	PFC0450w	28	CAA15614	99.0230	LVLLFIYKAY	2	371.7	10000001	207.5	1000000.0
MP03072	PFC0450w	59	CAA15614	99.0231	VLLFIYKAYK	01	10000000	10000000	31.2	10000001
MP03072	PFC0450w	19	CAA15614	99.0232	LFIYKAYKNK	01	1000000.0	10000000	434.4	1000000.0
MP03072	PFC0450w	72	CAA15614	99.0233	KLYTNFFMKK	10	10000001	10000001	5.8	1000000
MP03072	PFC0450w	33	CAA15614	99.0234	STYLSASDEY	9	57.2	10000001	85.1	10000001
MP03072	PFC0450w	36	CAA15614	99.0351	SQAHRENGK	0	62339.9	10000000	230.0	10000001
MP03072	PFC0450w	46	CAA15614	99.0352	ALVVAIILY	6	9.9	1000000.0	95.4	1000000.0
MP03072	PFC0450w	57	CAA15614	99.0353	FLVLLFIYK	0	14940.5	10000000	9.0	10000001
MP03072	PFC0450w	28	CAA15614	99.0354	LVLLFIYKA	6	13.1	102.2	132.5	10000001
MP03072	PFC0450w	99	CAA15614	99.0355	LLFIYKAYK	6	59055.3	10000001	9.6	10000001
MP03072	PFC0450w	62	CAA15614	99.0356	FIYKAYKNK	0	35013.8	10000001	22.0	10000001
MP03072	PFC0450w	22	CAA15614	99.0357	KLYTNFFMK	6	7491.5	10000001	2.3	10000001
MP03072	PFC0450w	74	CAA15614	99.0358	YTNFFMKKR	6	18478.3	10000001	48.4	10000001
45.t00001	Chromosome14	20		99.0235	ALERLISLKK	2	10000001	10000001	149.5	10000000
45.t00001	Chromosome14	109		99.0236	KILIKIPVTK	9	10000001	10000001	30.2	10000000
45.t00001	Chromosome14	128		99.0237	RLPLLPKTWK	9	1000000.0	10000001	9.61	10000001
45.t00001	Chromosome14	147		99.0238	NIFLRFIPDK	01	10000001	10000001	24.9	10000001
45.t00001	Chromosome14	191		99.0239	SQVSNSDSYK	9	1000000.0	10000001	36.0	1000000.0
100000	;									

Table 5: Pf-derived A3,11 supertype peptides scoring positive on PIC algorithm

Malaria locus	Addn Source info	Position	Accession No.	Peptide No.	Sequence	*	A*0101	A*0201 PIC	A*1101 PIC	A*2402
45.t00001	Chromosome14	249		99.0241	IIALLIIPPK	2	1000000.0	1000000.0	19.3	1000000.0
45.t00001	Chromosome14	374		99.0242	SQDLACIFDA	2	226.7	389.1	400.3	10000001
45.t00001	Chromosome14	34		99.0359	AVIFTPIYY	0	9.2	10000000	4.7	10000001
45.t00001	Chromosome14	20		99.0360	ALERLLSLK	0	6245.7	10000001	55.5	10000000
45.t00001	Chromosome14	88		99.0361	SISGKYDIK	0	29562.3	10000001	25.1	1000000.0
45.t00001	Chromosome14	101		99.0362	ILCIEGEQK	6	51943.1	10000001	162.5	1000000.0
45.t00001	Chromosome14	126		99.0363	EQRLPLLPK	6	66848.0	10000000	244.3	10000001
45.t00001	Chromosome14	148		99.0364	IFLRFIPDK	6	170326.8	10000000	112.0	10000000
45.t00001	Chromosome14	250		99.0365	IALLIIPPK	6	47443.5	1000000.0	25.2	10000000
45.t00001	Chromosome14	270		99.0366	<b>PVVCSMEYK</b>	6	20870.3	10000001	23.1	10000001
45.t00001	Chromosome14	172		99.0367	VVCSMEYKK	6	24792.5	1000000.0	8.3	10000000
45.t00001	Chromosome14	308		99.0368	FSYDLRLNK	0	5228.9	1000000.0	13.4	10000001
45.t00001	Chromosome14	323		99.0369	HLNIPIGFK	0	25082.0	10000000	98.3	10000001
MP03137	PFC0700c	14	CAB11150	99.0243	SSPLFNNFYK	2	10000001	1000000.0	0.5	10000001
MP03137	PFC0700c	151	CAB11150	99.0244	FLYLLNKKNK	2	10000001	10000000	139.2	10000001
MP03137	PFC0700c	183	CAB11150	99.0245	LQMIMINVILQK	2	10000001	10000000	83.6	10000001
MP03137	PFC0700c	195	CAB11150	99.0246	LTNHLINTPK	01	427675.0	0.0000001	20.8	10000001
MP03137	PFC0700c	259	CAB11150	99.0247	IFISFYLINK	01	10000001	10000001	102.0	1000000.0
MP03137	PFC0700c	293	CAB11150	99.0248	RLFEESLGIR	10	923199.1	10000001	420.0	10000001
MP03137	PFC0700c	91	CAB11150	99.0370	PLFNNFYKR	6	11760.5	10000001	383.0	10000001
MP03137	PFC0700c	141	CAB11150	99.0371	YQNFQNADK	6	40121.5	10000001	637.4	1000000.0
MP03137	PFC0700c	184	CAB11150	99.0372	QMMNVNLQK	6	17662.1	10000001	1.4	10000001
MP03137	PFC0700c	222	CAB11150	99.0373	AVSEIQNNK	6	0.1669	10000001	3.1	10000000
MP03137	PFC0700e	236	CAB11150	99.0374	GTMYILLKK	6	986.2	1000000.0	0.5	10000001
MP03137	PFC0700c	260	CAB11150	99.0375	FISFYLINK	6	7376.0	10000001	12.2	1000000.0
MP03137	PFC0700c	264	CAB11150	99.0376	YLINKHWQR	6	39562.3	10000001	41.6	1000000.0
MP03137	PFC0700c	273	CAB11150	99.0377	ALKISQLQK	6	37884.8	10000001	5.1	1000000.0
MP03137	000000									

Pf-derived A3,11 supertype peptides scoring positive on PIC algorithm

Malaria locus	Addn Source info	Position	Accession No.	Peptide No.	Sequence	¥	A*0101	A*0201 PIC	A*1101 PIC	A*2402
12.t00018	Chromosome14	68		99.0249	QLKHFFNSNK	2	1000000.0	10000000	33.5	1000000.0
12.t00018	Chromosome14	615		99.0250	YVSMYIPFIK	10	301060.0	10000000	5.6	1000000.0
12.t00018	Chromosome14	671		99.0251	VLFYIYNMYH	10	900700.0	10000000	13.6	1000000.0
12.00018	Chromosome14	705		99.0252	YTYIFFNYDK	01	742244.6	10000001	2.1	10000000
12.t00018	Chromosome14	1140		99.0253	SFFITYSYWK	2	10000001	10000001	5.7	100000000
12.100018	Chromosome14	195		99.0379	STSNKHINR	6	8.6099	10000000	3.8	10000000
12.100018	Chromosome14	687		99.0380	SQCNDYYIK	6	95255.3	10000001	6.3	10000000
12.100018	Chromosome14	968		99.0381	SSIFYIKNK	0	41588.5	1000000.0	8.4	1000000.0
12.00018	Chromosome14	1020		99.0382	LFFREKFLK	6	89243.3	1000000.0	14.3	1000000.0
12.t00018	Chromosome14	1160		99.0383	ILDNVSFLK	6	7621.1	100000000	21.0	1000000.0
mal_BU121g9.q1c1		92		99.0254	ILVLDIPGFK	으	10000000	10000000	55.0	10000000
mal_BU121g9.q1c1		45		. 99.0255	ETYGDSLVLH	10	453286.5	10000000	386.1	10000000
mal_BU121g9.q1c1		29		99.0256	EVGYFKRIFK	10	10000001	1000000.0	20.4	1000000
mal_BU121g9.q1c1		Ξ		99.0384	LVLDIPGFK	6	13172.2	1000000.0	26.7	1000000.0
mal_BU121g9.q1c1		30		99.0385	<b>GMLTVAGPR</b>	6	54761.5	1000000.0	326.1	1000000.0
mal_BU121g9.q1c1		39		99.0386	SQTELFETY	6	6.7	1000000.0	254.2	1000000.0
mal_BU121g9.qici		48		99.0387	GDSLVLHAK	6	19504.9	1000000.0	306.8	1000000.0
mal_BU121g9.q1cl		20		99.0388	SLVLHAKER	6	133501.5	1000000.0	487.4	1000000.0
ma_BU121g9.q1c1		99		99.0389	VGYFKRIFK	6	44416.3	10000000	27.9	1000000.0
mal_BU121g9.qlcf		98		99.0390	NIYIYIYIY	6	40.2	10000000	322.7	1000000.0
mal_BU121g9.qici		88		99.0391	YIYIYIYIY	6	16.2	1000000.0	310.0	1000000.0
mal_9A57b11.q1t2		31		99.0257	SSFNCDIANK	10	100000000	1000000.0	8.4	10000000
mal_9A57b11.q1c2		49		99.0258	SMGVFCLKEK	2	1000000.0	1000000.0	24.6	1000000.0
mal_9A57b11.q1c2		119		99.0259	HIVKNRIYNK	9	1000000.0	1000000.0	51.7	1000000.0
mal_9A57b11.q1t2		128		99.0260	KLKLHKJIRK	9	1000000.0	1000000.0	64.9	1000000.0
mal_9A57b11.q1t2		165		99.0261	FIFDIFKYAR	01	10000000	1000000.0	148.8	1000000.0
mal_9A57b11.q1t2		202		99.0262	AQKALSNLHK	2	10000000	1000000.0	113.8	10000000
mal 9A57b11.q1t2		208		99.0263	NLHKSWLQYK	2	507559.4	1000000.0	9'661	10000000

Table 5: Pf-derived A3,11 supertype peptides scoring positive on PIC algorithm

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Malaria locus	Addn Source info	Position	Accession No.	Peptide No.	Sequence	₹	A*0101	A*0201 PIC	A*1101 PIC	A*2402
mal_9A57b11.q1t2		234		99.0264	YLPLFLMMEH	2	1000000.0	1000000.0	147.3	1000000.0
mal_9A57b11.q1t2		32		99.0392	SFNCDIANK	6	27329.1	1000000.0	35.4	1000000.0
mal_9A57b11.q1t2		62		99.0393	KINKKYNKK	6	40379.4	1000000.0	56.4	1000000.0
mal_9A57b11.q1t2		95		99.0394	ILNNKELFK	Φ.	13663.7	1000000.0	29.6	10000001
mal_9A57b11.q1t2		120		99.0395	IVKNRIYNK	6	25949.5	1000000.0	17.8	10000000
mal_9A57b11.q1t2		154		99.0396	LINSKVFCY	6	6.1	1000000.0	113.8	1000000.0
mal_9A57b11.q1t2		183		99.0397	RQKEFYPIK	6	127059.4	0.0000001	38.7	1000000.0
mal_BL50e8.p1ca_5		6		99.0265	SFLVVLVFNK	2	10000000	1000000.0	33.6	10000000
mal_BL50e8.plca_5		152		99.0266	STYMTPSAIK	9	10000000	0.0000001	2.8	10000001
mal_BL50e8.plca_5		929		99.0267	KLYGEFTMNK	10	1000000.0	10000001	13	10000001
mal_BL50e8.p1ca_5		907		99.0268	GVYYIFVYLR	01	1000000.0	1000000.0	3.7	10000000
mal_BL50e8.p1ca_5		115		99.0398	SQYSNYFDY	6	11.0	1000000.0	15.2	1000000.0
mal_BL50e8.plca_5		361		99.0399	LFITYFQQK	6	90294.9	10000001	50.9	10000001
mal_BL50e8.p1ca_5		409		99.0400	ATSWDEYPK	6	44148.4	1000000.0	0.8	10000000
mal_BL50e8.plca_5		752		99.0401	ASFAAHENK	6	11256.9	1000000.0	0.2	10000001
mal_BL50e8.plca_5		780		99.0402	MLKADYFIR	6	35925.9	1000000.0	61.1	1000000.0
mal_BL50e8.p1ca_5		618		99.0403	VLNPVTIPK	6	14931.7	1000000.0	9.6	10000000
M13S8h6.p1t_3		63		6970766	VSYIFFMSFK	01	1000000.0	1000000.0	0.4	1000000.0
M13S8h6.p1t_3		937		99.0270	MQKYFLHISK	20	1000000.0	1000000.0	37.5	10000000
M13S8h6.p1t_3		25		99.0404	STFFFFLSR	6	3848.4	10000000	0.1	1000000.0
M13S8h6.plt_3		\$		99.0405	LLLTFGVYY	6	7.22	1000000.0	157.5	10000000
M13S8h6.p1t_3		157		99.0406	KFLFRYKQK	6	941796.8	1000000.0	16.1	10000001
M13S8h6.p1t_3		394		99.0407	KVFIKGKGK	6	43309.1	1000000.0	3.8	1000000.0
M13S8h6.p1t_3		1449		99.0408	TYIWIILK	6	6990.4	1000000.0	1.6	1000000.0
M13S8h6.p1t_3		1534		99.0409	KFFFFVFFY	6	51.8	10000000	3.5	2.2
M13S8h6.p1t_3		1655		99.0410	KLLQKLISK	6	8661.9	1000000.0	53.4	1000000.0
MI3SSh6 nlt 3										

Table 5: Pf-derived A3,11 supertype peptides scoring positive on PIC algorithm

Malaria locus 585.t00002 585.t00002 585.t00002 585.t00002	Addn Source info	Position	Accession					100004	A*1101	A*2402
\$85.t00002 \$85.t00002 \$85.t00002 \$85.t00002 \$85.t00002	The second secon		Ö.	Peptide No.	Sequence	\$	A*0101	PIC	<u></u>	
\$85.t00002 \$85.t00002 \$85.t00002 \$85.t00002	Chromosomel 1	193		99.0412	SQNNFSKIK	٥	90378.2	1000000.0	9.1	1000000.0
585.t00002 585.t00002 585.t00002	Chromosome11	300		99.0413	SSLNIYNTK	6	46908.8	0.0000001	5.2	1000000
585.t00002 585.t00002	Chromosome11	529		99.0414	KLFNYKFFK	6	60297.3	10000001	1.0	1000000.0
\$85.t00002	Chromosome11	572		99.0415	LTFLSNIRK	6	13099.9	10000001	1.3	10000001
	Chromosomel 1	919		99.0416	KFFYIFHYK	0	49030.6	10000001	0.7	10000000
585.t00002	Chromosomel 1	1415		99.0417	VTCSYFIIR	6	6831.4	10000001	16.8	10000001
S85.t00002	Chromosome11	1487		99.0418	LTCAFKIYK	6	25752.8	10000000	03	10000000
585.100002	Chromosomel 1	1508		99.0419	LFILFFIK	0	9492.2	10000000	1.2	1000000.0
585.t00002	Chromosome11	1541		99.0420	NLYFFIHNR	6	13239.8	10000000	59.3	1000000.0
585.t00002	Chromosome11	1742		99.0421	IFLHYYFKK	6	118461.5	10000000	9.2	10000001
1223.t00015	mal_9A21f9.q1t_4	4294		99.0271	QVFFLQEMER	2	544655.4	10000000	27.6	10000000
1223.t00015	mal_9A21f9.q1t_4	272		99.0422	SFYKFEVEK	9	193104.9	100000000	16.1	1000000.0
1223.t00015	mal_9A21f9.q1t_4	325		99.0423	KTFREHFLK	6	17344.2	10000001	0.022	10000001
1223.400015	mal_9A21f9.q1t_4	992		99.0424	VSNSSQLFK	6	13528.2	10000000	5.1	10000001
1223.t00015	mal_9A21f9.q1t_4	1397		99.0425	SLLNDVFPK	6	67376.3	10000000	1.2	10000001
1223.t00015	mal_9A21f9.q1t_4	1627		99.0426	KLFIFYLDK	6	25288.3	10000001	0.67	100000001
1223.100015	mal_9A21f9.q1t_4	1664		99.0427	LLNSQIIQY	6	18.6	10000000	160.0	10000001
1223.t00015	maf_9A21f9.q1t_4	2115		99.0428	FQGFYFLDK	6	6204.2	10000000	44.3	1000000.0
1223.100015	mal_9A21f9.q1t_4	2412		99.0429	NTFSFSWMK	6	16414.9	10000001	0.20	10000001
1223.100015	mal_9A21f9.q1t_4	4500		99.0430	MFYNCPVYK	6	327575.1	1000000.0	10.3	100000001
599.100001	Chromosomel 1	723		99.0272	NLLRHAIFYK	10	1000000.0	10000000	7.4	1000000.0
599.100001	Chromosome11	1288		99.0273	SSYGYNIYFK	01	1000000.0	10000001	0.3	10000001
599.t00001	Chromosome11	1451		99.0274	RTYVNEYFLR	01	1000000.0	10000001	25.4	1000000.0
599.t00001	Chromosome11	91		99.0431	ILLTLVFQK	6	46527.3	10000000	2.9	10000001
599.t00001	Chromosomel 1	28		99.0432	CONSLNYSK	0	38238.7	10000000	63.2	10000001
599.t00001	Chromosomel 1	211		99.0433	IVNNTELNK	6	9493.8	10000000	3.6	10000001
599.t00001	Chromosome11	776		99.0434	TLFSQNLFY	6	10.5	10000000	75.0	10000001
599.100001	Chromosome! I	1320		99.0435	TFYESVFTR	6	63945.9	10000001	27.9	10000001

Table 5: Pf-derived A3,11 supertype peptides scoring positive on PIC algorithm

Malaria locus	Addn Source info	Position	Accession No.	Peptide No.	Sequence	¥	A*0101	A*0201 PIC	A*1101 PIC	A*2402
599.100001	Chromosomel 1	1370		99.0436	YFFEEFFNK	٥	19717.0	1000000.0	4.6	10000000
100001.668	Chromosome! 1	1903		99.0437	TTQSNNIYK	δ	20011.8	1000000.0	2.1	1000000.0
MP01072	M1045c5.p1c.C_6	1451		99.0275	SLFYFTSNGK	2	10000001	1000000.0	8.0	1000000.0
MP01072	M1045c5.p1c.C_6	46		99.0438	KLNYDNFEK	0	48445.0	1000000.0	3.4	1000000.0
MP01072	M1045c5.p1c.C_6	327		99.0439	ILCDDGIYR	<u>ه</u>	19413.7	1000000.0	65.3	10000001
MP01072	M1045c5.plc.C_6	359		99.0440	KVADVFLQH	6	6428.6	1000000.0	4.4	1000000.0
MP01072	M1045c5.plc.C_6	419		99.0441	STSFLFLRK	6	2370.1	10000000	0.7	1000000.0
MP01072	M1045c5.p1c.C_6	421		99.0442	SFLFLRKQK	6	408258.6	1000000.0	12.7	10000001
MP01072	M1045c5.plaC_6	558		99.0443	SFFSSCENK	0	55537.2	10000000	17.7	10000001
MP01072	M1045c5.p1c.C_6	609		99.0444	AQSSYIYNK	6	18056.8	1000000.0	2.5	1000000.0
MP01072	M1045c5.p1c.C_6	1027		99.0445	<b>MSAKYLYHK</b>	ο,	5370.6	10000000	8.8	1000000.0
MP01072	M1045c5.p1c.C_6	1047		99.0446	TTLESHFNK	6	10524.0	10000000	0.2	10000001
MP01072	M1045c5.plc.C_6	1215		99.0447	SVYYNTMLR	6	. 6'9586	10000000	12	10000001
PIR2	T28161	1124		99.0276	VVNFLFELYK	02	408697.6	10000000	3.5	1000000.0
PIR2	T28161	1403		99.0277	TFFLWDRYKK	2	100000001	10000001	0.6	1000000.0
PIR2	T28161	801		99.0448	SVGACAPYR	6	59804.6	10000000	2.1	1000000.0
PIR2	128161	204		99.0449	KQLEDNLRK	6	87893.1	10000000	16.9	10000001
PIR2	T28161	758		99.0450	<b>KVASNMHHK</b>	6	6948.7	10000000	9'1	1000000.0
PIR2	T28161	260		99.0451	ASNMHHKKK	6	32965.2	10000001	4.3	1000000.0
PIR2	T28161	838		99.0452	AGFISNTYK	6	154161.8	1000000.0	2.2	10000001
PIR2	128161	965		99.0453	ILAFKEIYK	ο,	14274.5	10000000	12.6	1000000.0
PIR2	T28161	1879		99.0454	ALFKRWLEY	6	3.4	10000001	27.4	10000001
PIR2	128161	2151		99.0455	AFTYFYLKK	6	40565.6	10000000	9.1	10000001
55.t00004	Chromosome14	483		99.0278	FFFSNVNNNK	2	409139.5	10000000	408.4	10000001
55.t00004	Chromosome14	564		99.0279	SQGKKNTYLK	01	1000000.0	10000000	13.0	10000001
55.t00004	Chromosome14	926		99.0280	VFNNSIILEK	01	10000001	10000001	372.4	1000000.0
55.100004	Chromosome14	1338		99.0281	SVSEGYTSTY	0	8.79	10000001	33.5	10000001

Table 5: Pf-derived A3,11 supertype peptides scoring positive on PIC algorithm

Malaria locus	Addn Source info	Position	Accession No.	Peptide No.	Sequence	<b>\{</b>	A*0101	A*0201 PIC	A*1101 PIC	A*2402
55.t00004	Chromosome14	229		99.0456	TSICKYWIK	6	8242.3	1000000.0	14.6	1000000.0
55.t00004	Chromosome14	263		99.0457	TTICKHWKK	6	4558.7	1000000.0	1.7	10000000
55.t00004	Chromosome14	537		99.0458	KVTNVHIYK	6	41321.8	10000001	0.2	1000000
55.100004	Chromosome14	998		99.0459	ITNMNNINR	6	5371.8	10000001	37.6	1000000.0
\$5.100004	Chromosome14	606		99.0460	MLNIYKINK	6	17179.3	1000000.0	13.6	1000000.0
55.100004	Chromosome14	1030		99.0461	IINSYIDYK	6	84561.6	1000000.0	2.0	1000000
55.100004	Chromosome14	1141		99.0462	NLYTYVVNK	6	45076.1	1000000.0	54.8	1000000.0
55.t00004	Chromosome14	1665		99.0463	KMIYSIFIK	6	42191.9	10000000	4.1	1000000.0
13.100011	Chromosome14	8		99.0282	ISMDKSLFFK	10	10000000	10000000	16.7	1000000.0
13.t00011	Chromosome14	47		99.0283	TVFLDYVKGK	9	10000001	1000000.0	7.8	10000001
13.10001.1	Chromosome14	29		99.0284	DVYKETNIMNR	0	1000000.0	1000000.0	64.9	1000000.0
13.t00011	Chromosome14	117		99.0285	KLKKSTICNK	01	1000000.0	10000001	59.9	10000000
13.t00011	Chromosome14	6		99.0464	SMDKSLFFK	6	4208.2	1000000.0	3.5	1000000
13.t00011	Chromosome14	12		99.0465	KSLFFKSLK	6	64105.1	10000000	17.4	10000000
13.t00011	Chromosome14	48		99.0466	VFLDYVKGK	6	347222.4	1000000.0	216.7	1000000.0
13.t00011	Chromosome14	93		99.0467	KVKRFRVFK	6	52490.3	10000000	3.3	1000000.0
13.t00011	Chromosome14	104		99.0468	SFFIDEVKK	6	352606.0	1000000.0	37.8	10000000
13.t00011	Chromosome14	112		99.0469	KIYENKLKK	6	30696.4	10000001	14.5	1000000.0
37.t00002	Chromosome14	13		99.0286	ALTYMYCVYY	2	249.1	1000000.0	112.8	1000000.0
37.t00002	Chromosome14	31		99.0287	SQISIFCNLR	10	10000001	1000000.0	226.6	10000000
37.t00002	Chromosome14	32		99.0288	<b>QISIFCNLRR</b>	0	301919.5	10000001	80.8	10000001
37.t00002	Chromosome14	62		99.0289	VCNNETYYNK	01	1000000.0	10000001	186.8	10000001
37.t00002	Chromosome14	71		99.0290	KAHEENDKVK	01	1000000.0	1000000.0	956.7	1000000.0
37.t00002	Chromosome 14	13		99.0470	ALTYMYCVY	6	9.1	10000001	279.6	10000001
37.t00002	Chromosome14	32		99.0471	QISIFCNLR	6	26897.2	10000001	855.0	10000001
37.t00002	Chromosome14	33		99.0472	ISIFCNLRR	6	37287.9	10000001	255.9	10000001
37 100002	71000000000000000000000000000000000000	;								

Table 5: Pf-derived A3,11 supertype peptides scoring positive on PIC algorithm

								PIC		
Malaria locus	Addn Source info	Position	Accession No.	Peptide No.	Sequence	¥¥	AA A*0101	A*0201 PIC	A*1101 PIC	A*2402
674.100001	Chromosome11	8		99.0291	LVEFIFLLLK	9	304423.1	1000000.0	13.7	1000000.0
674.t00001	Chromosome11	218		99.0292	SVFYNKEIIK	01	993500.3	10000001	4.5	1000000.0
674.t00001	Chromosomel 1	867		99.0293	SLKDFDMLLY	01	199.3	10000000	214.4	1000000.0
674.100001	Chromosome11	2		99.0474	NVNDRFVEK	6	13728.8	10000001	11.8	10000001
674.100001	Chromosome11	999		99.0475	TLSNSLPQK	6	36834.4	10000001	47.0	10000000
674.100001	Chromosome11	673		99.0476	YQINNFIHK	٥	12103.7	10000000	8.65	10000000
674.100001	Chromosomel 1	689		99.0477	NLTINNFQK	6	59129.2	10000000	40.3	1000000.0
674.100001	Chromosome11	1035		99.0478	KFNRDMLQK	0	254779.4	10000001	1.9	1000000.0
674.t00001	Chromosome! 1	1126		99.0479	NQSDFLLLK	6	8015.9	10000001	15.2	10000000
674.100001	Chromosome11	1256		99.0480	SFHHFNIDK	6	178323.3	10000001	26.2	10000000
674.100001	Chromosome11	1288		99.0481	KSKELLLQK	6	27230.7	100000000	4.4	10000000

Table 6: Pf-derived 15mer peptides with nonamer core sequences scoring DR1 PIC <4nM

Antigen	Addn Source info	Position	No.	Sequence	¥	DR1 PIC
331.400003	Chromosome10	182	100:001	LSHFKKNFILQNNEE	15	0.447
331.t00003	Chromosome10	365	100.0002	TTFLSALKLLKIAQY	15	0.400
331.100003	Chromosome10	428	100.0003	NNKLSKNLSQLVHFY	15	0.130
331.t00003	Chromosome10	617	100.0004	KIYMFGGFSKGVRNN	15	0.061
331.t00003	Chromosome10	894	100.0005	DDMIGMPNLSSTVVC	15	0.337
331.t00003	Chromosome10	286	100.0006	<b>TFTFQNMYVRSKVVS</b>	15	0.400
331.100003	Chromosome10	1365	100.001	KYEIIGNILIFHYKY	15	0.435
331.100003	Chromosome10	1601	100.0008	KERMKNMYIVSNNDD	15	0.013
331.100003	Chromosome10	9591	100.000	GVGYFTLPLLKCIEA	15	0.302
331.t00003	Chromosome10	1725	100.0010	HRIILGLLPHSQPAW	15	0.167
Chr12Contig18	18.000811	13	100.001	HFFLFLLYILFLVKM	15	1.826
Chr12Contig18	18.000811	91	100.0012	LFLLYILFLVKMNAL	15	0.593
Chr12Contig18	18.000811	21	100.0013	ILFLVKMNALRRLPV	15	0.035
Chr12Contig18	18.000811	27	100.0014	MNALRRLPVICSFLV	15	3.206
Chr12Contig18	18.000811	22	100.0015	SAFLESQSMNKIGDD	15	3.392
Chr12Contig18	18.000811	132	100.001	<b>LKELIK VGLPSFENL</b>	15	0.785
Chr12Contig18	18.000811	143	100.0017	FENLVAENVKPPKVD	15	0.854
Chr12Contig18	18.000811	148	100.0018	AENVKPPKVDPATYG	13	3.392
Chr12Contig18	18.000811	158	100.001	PATYGIIVPVLTSLF	15	0.221
Chr12Contig18	18.000811	191	100.0020	YGIIVPVLTSLFNKV	15	0.956
MY924Fe3.p1t1		1015	100.0021	SVDLQIKISMKVLNS	13	0.103
MY924Fe3.plt1		1021	100.0022	KISMKVLNSMFHIIM	15	0.234
MY924Fe3.plt1		1076	100.0023	KDVVQIQTVLLSLGF	15	990'0
MY924Fe3.plt1		1331	100.0024	SQIIILPSILENIL	15	0.092
MY924Fe3.p1t1		1526	100.0025	MHSVKEMIVYLIQNN	15	0.262
MY924Fe3.p1t1		1703	100.0026	TINLINELMKRQHDK	15	0.192
MY924Fe3.p1t1		1746	100.0027	REMLLKMKSMSRNQR	13	0.130
MY924Fe3.p1t1		1878	100.0028	RSIIFAGHTIELNSL	15	0.248
MY924Fe3.plt1		1000	000001	NICE MEVOTOCO ACD D	71	1700

Table 6: Pf-derived 15mer peptides with nonamer core sequences scoring DR1 PIC <4nM

Antigen	Addn Source info	Position	No.	Sequence	₹	DR1 PIC
MY924Fe3.plt1		2201	100.0030	NLIITYLLIKKVLHN	15	0.162
MP03001	MAL3P2.11	-	100.0031	MRKLAILSVSSFLFV	15	2.786
MP03001	MAL3P2.11	36	100.0032	ELNYDNAGTNLYNEL	15	1.040
MP03001	MAL3P2.11	342	100.0033	QVRIKPGSANKPKDE	15	0.460
1369.t00001	Chromosome 11	28	100.0034	LLKIWKNYMKIMNHL	15	0.328
1369.t00001	Chromosome 11	43	100.0035	MTLYQIQVMKRNQKQ	15	0.056
1369.t00001	Chromosome 11	57	100.0036	QKQVQMMIMIKFMGV	15	0.016
1369.t00001	Chromosome 11	63	100.0037	MIMIKFMGVIYIMII	12	0.545
1369.t00001	Chromosome 11	20	100.0038	GVIYIMIISKKMMRK	115	0.076
1369.t00001	Chromosome 11	285	100.0039	LYYLFNQHIKKELYH	15	0.742
1369.t00001	Chromosome 11	299	100.0040	HFNMLKNKMQSSFFM	15	0.560
1369.t00001	Chromosome 11	353	100.0041	XDIYQKLYIKQEEQK	15	0.807
1369.100001	Chromosome 11	366	100.0042	QKKYIYNLIMNTQNK	15	0.167
1369.t00001	Chromosome 11	381	100.0043	YEALIKLLPFSKRIR	15	0.701
699.t00001	Chromosome 11	265	100.0044	NIHFAVLFLTLTVYP	15	0.347
100001	Chromosome 11	269	100.0045	AVLFLTLTVYPINNF	15	0.255
699.t00001	Chromosome 11	623	100.0046	KLLYKMNYLKQDINN	15	0.545
699.t00001	Chromosome 11	744	100.0047	KKEFKNSLILLNLYN	15	0.576
699.100001	Chromosome 11	773	100.0048	YLSFKILNTLLYNHI	15	0.234
699.t00001	Chromosome 11	998	100.0049	IYILINHVIIPSLFY	15	0.400
100001	Chromosome 11	875	100.0050	IPSLFYLYMNFLKFI	15	0.347
699.t00001	Chromosome 11	929	100.001	KYLIILLYIFKLIEY	15	0.701
100001669	Chromosome 11	846	100.0052	<b>FIFMQNNQTKLAEMK</b>	15	0.039
100001	Chromosome 11	1032	100.0053	LFIYIWLHLIIIFIF	15	0.423
mal_4T2c4.pltl		15	100.0054	ILLIRPMLVKLRPKL	15	0.221
mal_4T2c4.p1t1		19	100.0055	RPMLVKLRPKLVKLR	15	0.083
mal_4T2c4.plt1		56	100.0056	RPKLVKLRPMLVKLG	15	0.010
mal_4T2c4.p1t1		33	100.0057	RPMLVKLGPILVKLR	15	0.004
mai 472c4 plt1		4	000000		:	0.00

Table 6: Pf-derived 15mer peptides with nonamer core sequences scoring DR1 PIC <4nM

Antigen	Addn Source info	Position	Peptide No.	Sequence	\$	DR1 PIC
mal_4T2c4.p1t1		47	100.0059	RPMLVKLRPMLAKLR	52	0.016
mal_4T2c4.plt1		\$2	100.0060	RPMLAKLRPMLAKLR	15	0.027
mal_4T2c4.plt1		19	100.001	RPMLAKLRPKLVKLR	15	0.137
mal_4T2c4.plt1		89	100.0062	RPKLVKLRPKLVKLR	15	0.083
mal_4T2c4.p1t1		75	100.0063	RPKLVKLRPISVNAK	15	0.076
M13Hg2.q1t3		68	100.0064	ILEMKPNILLSRFIF	15	0.742
M13Hg2.q1t3		122	100.0065	<b>NISINNAFSLPVNIY</b>	15	0.663
M13Hg2.q1G		163	100.0066	YFNIIQQKIQSNFLL	15	0.487
M13Hg2.q1t3		182	100.0067	ISTFIKNNINHQENN	15	0.682
M13Hg2.q1G		442	100.0068	LKNMDGNILIKDFIQ	15	0.378
M13Hg2.q1t3		488	100.0069	<b>IEFYNINMAKKVMNN</b>	15	0.285
M13Hg2.q1t3		492	100.0070	NINMAKKVMNNMEKN	15	0.145
M13Hg2.q1t3		558	100.001	FVNYFEAVVHMNIHC	15	0.831
M13Hg2.q1t3		169	100.0072	NNNIINGHWLEQKLS	15	0.123
M13Hg2.q1t3		869	100.0073	NNDMKKGYTNVSNNS	15	0.162
Mal_5L10c4.q1t6		154	100.0074	NNEFFGYPLQFVCET	15	0.255
Mal_5L10c4.q1t6		336	100.0015	FFIIKNVGVHKITYY	15	0.388
Mal_5L10c4.q1t6		1090	100.0016	KIEYISMLSPTINEI	15	0.113
Mal_5L10c4.q1t6		1101	100.001	INEIKTLNTILTIPL	15	0.018
Mal_5L10c4.q1t6		1107	100.0018	LNTILTIPLIKMNEY	15	0.042
Mal_5L10c4.q1t6		1264	100.0019	HKLFINKLMTSNIRK	15	0.203
Mal_5L10c4.q1t6		1289	100.0080	<b>QNRFRNQLLYLTKIA</b>	15	0.050
Mal_5L10c4.q1t6		1609	100.001	IKKIKTPLILPIDPN	15	0.035
Mal_5L10c4.q1t6		1888	100.0082	QDHLVIQIIYVMDNI	15	0.133
Mal_5L10c4.q1t6		2031	100.0083	<b>IEAMGGAHSIGYEQF</b>	15	0.068
571.t00003	Chromosome11	33	100.0084	FDDFKINYSYKTKNH	15	0.182
571.t00003	Chromosome11	462	100.0085	ITDLNNMNVNQSNMK	15	0.500
571.100003	Chromosome11	096	100.0086	TNNFNNNVMMLMNTS	15	0.007
571 +00003			1			

Table 6: Pf-derived 15mer peptides with nonamer core sequences scoring DR1 PIC <4nM

100,0088 AQNVAQNVAQNVEQN 100,0089 SNKFMTPTTLKEKYQ
100.0090
100.0091
100.0093
100.0094
100.0095
100.0096
100.0097
100.0098
100.0099
100.0100
100.0101
100.0102
100.0103
100.0104
100.0105
100.0106
100.0107
100.0108
100.0109
100.0110
100.0111
100.0112
100.0113
100.0114
100.0115

Table 6: Pf-derived 15mer peptides with nonamer core sequences scoring DR1 PIC <4nM

Antigen	Addn Source info	Position	Peptide No.	Sequence	₹	DR1	PIC
MP03137	PFC0700c	180	100.0117	VLFLQMMNVNLQKQL	2	90	990.0
MP03137	PFC0700c	187	100.0118	NANLQKQLL TNHLIN	15	0.0	0.956
MP03137	PFC0700c	161	100.0119	QKQLLTNHLINTPKI	15	Ξ	1.132
MP03137	PFC0700c	161	100.0120	NHLINTPKIMPHHII	15	0.5	0.576
MP03137	PFC0700c	239	100.0121	YILLKKILSSRFNQM	15	=	1.100
MP03137	PFC0700c	250	100.0122	FNQMIFVSSIFISFY	15	2.420	70
12.t00018	Chromosome14	36	100.0123	CNILKENNTYKQKKH	15	4.016	91
12.t00018	Chromosome14	133	100.0124	TNELKKMDTKKDVHM	15	1.011	=
12.t00018	Chromosome14	504	100.0125	EVKFILHMTLLTLYK	15	0.269	69
12.t00018	Chromosome14	542	100.0126	KYNFLNIYASLRNEY	15	0.328	82
12.100018	Chromosome14	583	100.0127	TRCFKNSYPKKVWKK	15	0.293	83
12.t00018	Chromosome14	612	100.0128	NNLYVSMYIPFIKKF	15	0.411	=
12.t00018	Chromosome14	1000	100.0129	EAKFKIERLLKSSYK	15	3.298	86
12.t00018	Chromosome14	1057	100.0130	KIYILNNNLLIVHLS	15	1.543	£
12.t00018	Chromosome14	1184	100.001	KCSFDKTNPIQQSGK	15	2.044	4
12.t00018	Chromosome14	1212	100.0132	TGIFNMPNLVQINNY	15	0.078	82
mal_BU121g9.q1c1		53	100.0133	EGMLTVAGPRSQTEL	15	3.298	86
mal_9A57b11.q1t2		m	100.0134	KQNIKYTQIISIDNI	15	2.633	33
mal_9A57b11.q1t2		<u>«</u>	100.0135	· LNKIADPILIGFSSS	15	0.929	67
mai_9A57b11.q1t2		123	100.0136	NRIYNKLKLHKIIRK	15	1.267	22
mal_9A57b11.q1t2		194	100.0137	NNEYGILNAQKALSN	15	0.098	86
mal_9A57b11.q1t2		161	100.0138	YGILNAQKALSNLHK	15	0.141	=
mal_9A57b11.q1t2		229	100.0139	KIFVKYLPLFLMMEH	15	0.042	2
mal_9A57b11.q1t2		236	100.0140	PLFLMMEHSFLNCHK	15	3.031	<del></del>
mal_BL50e8.pica_5		-	100.0141	MEGFVALLSFLVVLV	15	0.004	*
mal_BL50e8.plca_5		100	100.0142	VDGMKIGHPISVALG	15	0.010	9
mal_BL50e8.plca_5		151	100.0143	<b>GSTYMTPSAIKIKVP</b>	15	0.057	72
mal_BL50e8.plca_5		189	100.0144	NNLFIYNWVLQTSSP	15	0.560	9
mal BL50e8.plca 5		347	100.0145	EKILIRALI SLIDESI.	15	0.77	2

Table 6: Pf-derived 15mer peptides with nonamer core sequences scoring DR1 PIC <4nM

Antigen	Addn Source info	Position	No.	Sequence	\$	DRI
mal_BL50e8.plca_5		437	100.0146	HPVYPTAPAVAFPAG	2	0.187
mal_BL50c8.p1ca_5		585	100.0147	EVYYFPGKVTRVRAK	15	0.357
mal_BL50e8.p1ca_5		909	100.0148	EDKLVKIYISLLSSD	15	0.423
mal_BL50e8.p1ca_5		685	100.0149	IERYVGLGSFHFYLY	15	0.423
mal_BL50e8.p1ca_5		816	100.0150	CFQVLNPVTIPKYCI	15	0.285
M13S8h6.p1t_3		89	100.001	<b>FMSFKILEALLVCIS</b>	15	9000
M13S8h6.p1t_3		127	100.0152	KQIVIFLISLLSFTL	15	0.473
M13S8h6.p1t_3		691	100.0153	<b>AKQIEILHTMLPNFL</b>	15	0.095
M13S8h6.p1t_3		218	100.0154	IDDFQNMVSTLQPHV	15	0.034
M13S8h6.p1t_3		285	100.0155	KCAIKLAIAQLSAKY	15	0.130
M13S8h6.p1t_3		343	100.0156	IGSVKPQYALFGDTV	15	0.228
M13S8h6.p1t_3		871	100.0157	KIYIKKKRLLQMNNY	15	0.411
M13S8h6.p1t_3		1350	100.0158	KKLLKKLTSNLQLNK	15	9200
M13S8h6.p11_3		1602	100.0159	<b>QDFLTKILPRQVLEE</b>	15	0.241
M13S8h6.p1t_3		1754	100.0160	MWGLDVLIANKIESN	15	0.423
585.t00002	Chromosome11	S	100.001	FFILFYFYVMSTYTF	15	0.500
585.t00002	Chromosomel 1	16	100.0162	TYTFCFLPVLQTQLG	15	0.515
585.t00002	Chromosomel 1	349	100.0163	KKKYKNKKMPKTIDG	15	0.473
585.100002	Chromosome11	487	100.0164	GRAIIPLFLILNTYK	15	0.269
\$85.t00002	Chromosome11	295	100.0165	KIIFKRNPLFLTFLS	15	0.367
585.t00002	Chromosome11	643	100.0166	WLFFFDLVVLSPFSL	15	0.500
585.t00002	Chromosome11	774	100.0167	KNIIKGKNMMTRGGG	15	901'0
585.t00002	Chromosome11	962	100.0168	KMFIKGDTVMKANII	15	0.038
585.t00002	Chromosome11	1093	100.0169	VGSYKLMISQEAEFE	15	0.487
585.t00002	Chromosome11	1344	100.0170	LNRFITLITWTQHVS	15	0.095
1223.t00015	mal_9A21f9.q1t_4	1070	100.001	RTKYETLYTIHVHQR	15	0.087
1223.t00015	mal_9A21f9.q1t_4	1162	100.0172	GLCYGGAPAGPAGTG	15	0.059
1223.t00015	mal_9A21f9.q1t_4	1654	100.0173	DSILILQTINLLNSQ	15	0.177
1222 000015	91010					

Table 6: Pf-derived 15mer peptides with nonamer core sequences scoring DR1 PIC <4nM

Antigen	Addn Source info	Position	Peptide No.	Sequence	<b>₹</b>	DR1 PIC
1223.100015	mal_9A21f9.q1t_4	2779	100.0175	IDLYKQMYVKKYDEI	15	0.158
1223.t00015	mal_9A21f9.q1t_4	2878	100.0176	DKDLKAALPYLHEAE	15	0.103
1223.t00015	mal_9A21f9.q1t_4	2985	100.001	TIELLKPYIQSTFFK	15	0.145
1223.t00015	mal_9A21f9.q1t_4	2995	100.0178	STFFKTQIAKKASVA	15	0.002
1223.t00015	mal_9A21f9.q1t_4	3014	100.0179	CKWVGAMAMYNQASK	15	0.145
1223.t00015	mal_9A21f9.q1t_4	3019	100.0180	<b>AMAMYNQASKIVKPK</b>	15	0.116
599.100001	Chromosomel 1	12	100.001	NFFILTLVFQKYS	15	0.177
599,t00001	Chromosome11	364	100.0182	NNNLGIPTLIKKEVH	15	0.234
599.100001	Chromosome 11	819	100.0183	<b>EEDIKNAYLPENKNF</b>	15	0.435
599.t00001	Chromosome11	1074	100.0184	INVFIKEISKLFDHD	15	0.529
599.t00001	Chromosome11	1414	100.0185	DKSLKIMYSLFNKYT	15	0.098
100001665	Chromosome11	1463	100.0186	VVIFIYGNIIISDLK	15	0.645
599,100001	Chromosome11	1621	100.0187	CESFISKVTNKVIKK	15	0.215
599.t00001	Chromosome11	1740	100.0188	ICTFVKYITFQLLNI	15	0.854
599.100001	Chromosomel 1	1767	100.0189	KEHYIMNNTIFTFNQ	15	0.141
599.100001	Chromosomel 1	1892	100.0190	KKKYKYIPSNGTTQS	15	0.500
M1045c5.p1c.C_6		53	100.001	EKSLGILGSIQNAYL	15	0.085
M1045c5.p1c.C_6		29	100.0192	LGSIQNAYLYKSIFK	15	0.388
M1045c5.p1c.C_6		288	100.0193	SCIMNNMIVTKESNE	15	0.473
M1045c5.p1c.C_6		1040	100.0194	KDFMKNNTTLFSHFN	15	0.241
M1045c5.p1c.C_6		1136	100,0195	MLYLIRNILMSIEDY	15	0.435
M1045c5.p1c.C_6		1229	100.0196	KKKYIKLNIFKNIIL	15	0.378
M1045c5.p1c.C_6		1350	100.0197	RWDLVMNMMIGIRIS	15	0.054
M1045c5.p1c.C_6		1380	100.0198	HKDVIQLPTSNAQHK	15	0.167
M1045c5.plc.C_6		1393	100.0199	HKVIFKNYAPIIFKN	15	0.262
M1045c5.p1c.C_6		1430	100.0200	SNMVLGNLSTLSELL	15	0.423
PIR2	T28161	46	100.0201	AKFYNGGEIMQPNSK	15	0.153
PIR2	T28161	319	100.0202	KRNLKLQNAIKNCRG	15	0.043
PIR2	178161	1072	100 003	HAWIIIWII I IHGKEO	7	505.0

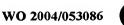
Table 6: Pf-derived 15mer peptides with nonamer core sequences scoring DR1 PIC <4nM

Antigen	Addn Source info	Position	No.	Sequence	₹	DR1	PIC
PIR2	T28161	1093	100.0204	KYKLLYLQAQTTAAN	15	0.141	
PIR2	T28161	1096	100.0205	LLYLQAQTTAANGGP	15	0.047	_
PIR2	T28161	1589	100.0206	SPKIVVPAPKPTTTF	15	0.119	_
PIR2	T28161	1951	100.0207	FVDLIRQIAATIDKG	15	0.047	_
PIR2	T28161	2065	100.0208	QERLVKNPLVQPTLK	15	0.028	~
PIR2	T28161	2129	100.0209	<b>HPAVIPALVTSTLAW</b>	15	0.072	٠.
PIR2	T28161	2419	100.0210	NELFGTNHVKQTSIH	15	0.098	~~
55.t00004	Chromosome14	<b></b>	100.0211	<b>NNEFVVAQLYELNNY</b>	15	1.340	_
55.100004	Chromosome14	117	100.0212	DNNMKKYLIQKCGKK	15	1.776	
55.t00004	Chromosome14	218	100.0213	SCSIIKYELRKTSIC	15	1.878	
55.100004	Chromosome14	385	100.0214	RNHMDKPPHNINNN	15	0.228	
55.t00004	Chromosome14	613	100.0215	NNNLIFQNSRFMDHT	15	0.423	
55.t00004	Chromosome14	754	100.0216	THDIIKNVSNNMKRF	15	0.357	_
55.t00004	Chromosome14	906	100.0217	FKNVDMLNIYKINKD	15	1.987	_
\$5.t00004	Chromosome14	1136	100.0218	MKDVINLYTYVVNKK	15	0.092	-1
55.t00004	Chromosome14	1364	100.0219	GMYILPQYVTRECIN	15	1.500	_
55.100004	Chromosome14	1510	100.0220	GDDVIYEETKKTDNI	15	1.587	_
13.t00011	Chromosome14	91	100.0221	FKSLKNNNMLESTGI	15	1.587	_
13.t00011	Chromosome14	49	100.0222	FLDYVKGKMMDVYKE	15	0.126	٠.
13.t00011	Chromosome14	25	100.0223	TYNYLTPTLKVKRFR	15	3.589	_
37.t00002	Chromosome14	20	100.0224	NDLIDQNIVYLNVCN	15	2.560	_
674.t00001	Chromosome! 1	30	100.0225	<b>LKKLKKILLNLDVLI</b>	15	0.742	
674.t00001	Chromosome11	25	100.0226	NENFDMELLNNVNDR	15	1.378	
674.t00001	Chromosomel 1	124	100.0227	NCPIKNEVTTLIQKI	15	0.367	_
674.100001	Chromosomel I	396	100.0228	EKNMTSQKSITSEKN	15	0.854	_
674.t00001	Chromosome11	27.7	100.0229	NSNFKEQHLLFCNNL	15	1.418	
674.100001	Chromosomel 1	752	100.0230	NNNIKTHIANFNIIH	15	1.040	_
674.t00001	Chromosome11	986	100.0231	NNLYKTYEMIQGDND	15	0.956	
.00000							

Table 6: Pf-derived 15mer peptides with nonamer core sequences scoring DR1 PIC <4nM

0.983	0.854
15	15
FLQYRIPHMNNGNI	VDIFCKIHALKNENK
100.0233	100.0234
1353	1432
Chromosome11	Chromosome11
674.100001	674.t00001
	Chromosomel 1 1353 100.0233

- **Claims**
- 1. An isolated and/or purified polynucleotide sequence comprising:
- a polynucleotide sequence encoding: 1) a polypeptide sequence selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27; or 2) a polypeptide as set forth in Tables 2, 3, 4, 5, or 6;
- a complementary polynucleotide sequence to: 1) a polynucleotide b) sequence encoding a polypeptide sequence selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27; or 2) a polynucleotide sequence encoding a polypeptide sequence as set forth in Tables 2, 3, 4, 5, or 6
- c) a polynucleotide sequence having at least about 20% to 99.99% identity to a polynucleotide sequence of 1(a) or 1(b);
  - d) a fragment of a polynucleotide sequence according to 1(a) or 1(b);
- e) a polynucleotide sequence encoding a variant of: 1) a polypeptide selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27; or 2) a polypeptide as set forth in Tables 2, 3, 4, 5, or 6;
- a polynucleotide sequence encoding a polypeptide fragment of a polypeptide selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27, wherein the fragment has substantially the same serologic reactivity as the native polypeptide and substantially the same T-cell reactivity as the native polypeptide or fragment;
- h) a polynucleotide sequence encoding a fragment of a variant polypeptide of a polypeptide selected from the group consisting of SEO ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27, wherein the fragment of the variant polypeptide has substantially the same serologic activity as the native polypeptide or substantially the same T-cell reactivity as the native polypeptide or fragment; or
  - a polynucleotide sequence encoding a multi-epitope construct. **i**)
- 2. A primer or detection probe for hybridization with a target sequence or the amplicon generated from a target sequence comprising a sequence of at least 8, 9, 10, 11,



- 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100 consecutive nucleotides of the polynucleotide sequences according to claim 1.
- 3. The isolated polynucleotide according to claims 1 or 2 further comprising a label.
- 4. The isolated polynucleotide according to claim 3, wherein said label is a: 1) radioactive label, 2) enzyme label, 3) chemiluminescent label, 4) fluorescent label, or 5) magnetic label.
- 5. The method of detecting *P. falciparum* in biological samples comprising contacting a biological sample with isolated polynucleotides of claim 1, 2, 3, or 4 and detecting the hybridization of said isolated polynucleotides with nucleic acids contained in said sample.
- 6. A DNA chip comprising polynucleotide sequences according to claims 1, 2, 3 or 4.
- 7. An isolated polynucleotide sequence according to claim 1 or 2, further comprising regulatory sequences.
- 8. The isolated polynucleotide sequence according to claim 7, wherein said regulatory sequences are promoters, enhancer elements, or termination sequences that are operably linked to said polynucleotide.
- 9. A vector comprising a promoter operably linked to a nucleic acid sequence according to claim 1.
- 10. The vector according to claim 9, wherein said vector contains one or more origins of replication.
- 11. The vector according to claim 10, wherein said vector contains one or more selectable markers.

- 12. The vector according to claim 9, wherein said vector contains one or more selectable markers.
- 13. The vector according to claim 9, wherein said vector is a vaccine vector or a viral vector.
- 14. A vector comprising a promoter operably linked to a nucleic acid sequence according to claim 2.
- 15. The vector according to claim 14, wherein said vector contains one or more origins of replication.
- 16. The vector according to claim 15, wherein said vector contains one or more selectable markers.
- 17. The vector according to claim 14, wherein said vector contains one or more selectable markers.
- 18. The vector according to claim 14, wherein said vector is a vaccine vector or a viral vector.
- 19. A host cell transformed by: 1) a vector according claim 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18; or 2) a polynucleotide according to claim 1, 2, or 7.
- 20. A composition comprising a pharmaceutically acceptable carrier and a polynucleotide according to claim 1, 2, 7, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18.
- 21. A method of inducing an immune response in an individual comprising the administration of a composition according to claim 20 in an amount sufficient to induce an immune response.
  - 22. An isolated polypeptide comprising:

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- a) SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27;
  - b) a polypeptide as set forth in Tables 2, 3, 4, 5, or 6;

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- c) a fragment of a polypeptide or a variant polypeptide of: a) a polypeptide set forth in SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27; or b) a polypeptide as set forth in Tables 2, 3, 4, 5, or 6, wherein said fragment or variant has substantially the same serologic reactivity or substantially the same T-cell-reactivity as the native polypeptide;
- d) a variant polypeptide having at least about 20% to 99.99% identity to a polypeptide provided in Table 2, 3, 4, 5, or 6 or selected from the group consisting of SEQ ID NO: NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27;
  - e) a polypeptide epitope as set forth in Table 2, 3, 4, 5, or 6; or
- f) a multi-epitope construct: 1) comprising at least one epitope set forth in Table 2, 3, 4, 5, or 6; 2) comprising a polypeptide selected from the group consisting of SEQ ID NO: NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27 and at least one epitope set forth in Table 2, 3, 4, 5, or 6; or 3) comprising and at least one epitope set forth in Table 2, 3, 4, 5, or 6 and one or more polypeptide selected from the group consisting of SEQ ID NO: NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27.
- 23. The polypeptide epitope according to claim 22, wherein the polypeptide epitope is a CTL-inducing peptide epitope.
- 24. The polypeptide epitope according to claim 22, wherein the polypeptide epitope is a HTL-inducing peptide epitope.
- 25. The method for eliciting an immune response in an individual comprising the administration of a composition comprising polypeptides according to claim 22, 23, or 24 to an individual in amounts sufficient to induce an immune response in the individual.
- 26. A composition comprising a pharmaceutically acceptable carrier and a polypeptide according to claim 22, 23, or 24.

- 27. The composition according to claim 26, wherein said carrier is an adjuvant.
- 28. A method of detecting a *P. falciparum* antigen comprising contacting a biological sample obtained from an individual with a polypeptide according to the claim 22, 23, or 24 and detecting the formation of an antibody-antigen complex or detecting the stimulation of T-cells obtained from the individual.
- 29. An isolated antibody, or fragment thereof, that specifically binds to a polypeptide as set forth in claim 22, 23, or 24.

## SEQUENCE LISTING

<110> Epimmune, Inc.
 The United States of America as Represented by the
 Secretary of the Navy
 Sette, Alessandro
 Doolan, Denise L.
 Carucci, Daniel J.
 Sidney, John
 Southwood, Scott

- <120> PLASMODIUM FALCIPARUM ANTIGENS AND METHODS OF USE
- <130> EPI-103X
- <150> US 60/431,494
- <151> 2002-12-06
- <160> 27
- <170> PatentIn version 3.2
- <210> 1
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Ile Asn Gln Tyr Lys Asn Cys Leu Asp Gly Glu Lys Lys Leu Phe Leu 50 55 60

Asn Lys Cys Ile Lys Asn Gly Asn Val Lys Tyr Ile Glu Lys Val Val 65 70 75 80

Lys Gln Ile Ile Glu Lys Lys Asn Val Tyr Asn Asp Ile Asp Asp Lys

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Ser Ile Lys Lys Ser Ile Asp Leu Leu Ile Tyr Pro Cys Val Tyr Glu 100 105 110

Ile Asn Lys Asn Glu Phe Tyr Tyr Thr Thr Ser Cys Cys Ser Gly Arg 115 120 125 WO 2004/053086

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Ser Ala Leu Lys Leu Lys Ile Ala Gln Tyr Ala Gly Leu Lys Gln 375 Ser Gly Ile Leu Asn Phe Asn Lys His Val Thr Val Ala Ile Arg Gly 390 Ser Met Arg Leu Glu His Leu Leu Gly Asp Ile His Pro Thr Leu Gln 410 Gln Thr Asn Leu Met Glu Ile Ile His Ile Cys Asn Asn Lys Leu Ser Lys Asn Leu Ser Gln Leu Val His Phe Tyr Lys Cys Phe Lys Gln Phe Lys Glu His Glu His Thr Tyr Gln Phe Val Ser Ile Asn Arg Glu Met 455 Leu Ser Ser Leu Glu Asn Asn Leu Ser Ser Asn Thr Lys Gln Lys Lys 470 475 Lys Ser Asn Lys Lys Asn Thr Leu His Val Lys Asp Asn Leu Gln Asp 485 490 Asn Lys Lys Ile Ala His His Met Lys Lys Lys Lys Glu Ile Asn 500 505 His Leu Tyr Leu Thr Cys Ser Gly Lys Lys Asn Ile Pro Asn Gly Asn 515 520 Arg Ser Ile Ala Glu Gln Asp Lys Thr Glu Cys Lys Leu Lys Asp Glu 535 Ile Ile Tyr Glu Asn Thr Glu Asn His Ile Asn Ile Ile Lys Lys Glu 550 Lys Asn Ile Ile Asp Leu Asn Lys Tyr Asn Ile Gln Leu Asn Glu Glu 565 570 Gly Tyr Ile Ile Asn Glu Asn Lys Asn Asp Lys Phe Ile Gly Trp Lys 580 585 Ile Leu Gly Asn Asn Asn Met Asn Val Gln Asn Phe Phe Val Trp Gly

600

605

His Asp Met Phe Met Gln Glu Asn Lys Ile Tyr Met Phe Gly Gly Phe 610 Ser Lys Gly Val Arq Asn Asn Lys Leu Lys Ile Tyr Asp Ile Ile Asn 635 630 Lys Lys His Phe Ile Tyr Asp Thr Glu Leu Pro Ser Leu Val Phe His Asn Phe Val Gln Leu Asp Asp Lys Phe Ala Phe Ile Phe Gly Gly Arg 665 Gln Asn Pro Lys Asn Cys Thr Asn Met Val Trp Val Tyr Asn Ile Lys 680 Glu Asn Phe Trp Ile Lys Ala Arg Arg Thr Ser Thr Leu Val Arg Lys Asn Lys Asn Val Leu Phe Leu Glu Lys Met Glu Lys Asn Met Glu Val 710 715 Lys Met Asp Arg Met Lys Tyr His Met Gly Lys Lys Tyr Asn Asn Asp 725 730 745 Asn Asn Phe Leu Cys Asn Asp Glu Asn Ile Phe Tyr Phe Asn Asn Glu 760 Glu Glu Pro Cys Pro Arg Tyr Arg His Ala Ser Val Phe Val Arg Arg 775 Tyr Ile Lys Lys Ser Lys Ser Ile Tyr Ile Phe Tyr Thr Tyr Gly Gly 790 795 Val Asn Glu Lys Asn Glu Ile Leu Asn Asp Ile Trp Glu Gly Lys Ile 805 810 Ile Leu Asn Leu Glu Asp Lys Gly Ile Ala His Ile Glu Trp Asn Lys Lys Asn Cys Ser Gln Lys Thr Glu Ala Cys Arg Ile Asn Asn His Ser 835 840

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850 855 860

Gln Asp Asn Asp Lys Asp Asn Tyr Thr Gln Tyr Asn Glu Tyr Asn Asn 865 870 875 880

5

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Cys Leu Gly Asp Asp Asn Met Glu Leu Lys Ala Tyr Pro Ser Asp Arg 930 935 940

Phe Ser His Ser Thr Cys Leu Ile Asn His Asn Phe Phe Met Leu Val 945 950 955 960

Gly Gly Ile Asn Ile His Arg Thr Leu Asn Asp Val Trp Leu Phe His 965 970 975

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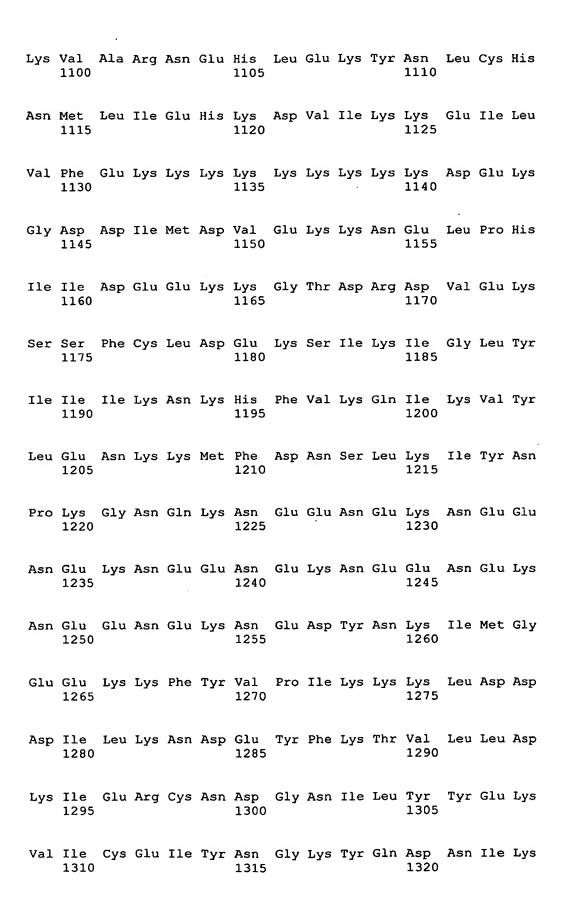
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Val Lys Glu Gly Gln Ala Thr Tyr Asn Asn Glu Ile Lys Lys Asn. . 1055 1060 1065

Asn Asn Asn Asn Lys Cys Ser Asn Asn Tyr Asn Ile Leu Val Asp 1085 1090 1095





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- Phe His Lys Phe Leu Asn Lys Lys Val Lys Asn Tyr Leu Asn Ser 1340 1345 1350
- Ser Glu Lys Lys Met Val Leu Gln Gly Tyr Arg Lys Tyr Glu Ile 1355 1360 1365
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- Lys Glu Val Lys Lys Phe Trp Leu Ala Ile Lys Asp Ile Phe Asn 1445 1450 1455
- Asn Lys Asp Ile Phe Asn Asn Lys Glu Ile Ile Leu Asn Thr Asn 1460 1465 1470
- Ile Leu Ser Leu Lys Lys Lys Lys Lys Glu Lys Lys Lys Lys Lys 1475 1480 1485
- Lys Asn Asn Asn Asn Lys Phe Tyr Val Lys Val Lys Phe Asn 1490 1495 1500
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Cys Val Ala Leu Tyr Glu Lys Val His Gly Lys Leu Arg Gln Asn Lys Ile His Ile Val Cys Gly Lys Asn Leu Lys Thr Val His Ile 1565 1570 Glu Asn Lys Ile Lys Tyr Lys Leu Asp Leu Thr Lys Cys Met Phe Ser Ser Gly Asn Gly Thr Glu Lys Glu Arg Met Lys Asn Met Tyr Ile Val Ser Asn Asn Asp Asp Asn Ile Asn Asn Lys Asp Lys Asn 1630 1635 Leu Asp Glu Lys Arg Asp Arg Val Lys Glu Asn Val Val Asp Leu Phe Cys Gly Val Gly Tyr Phe Thr Leu Pro Leu Leu Lys Cys Ile Glu Ala Gln Asn Lys Ile Asn Asn Tyr Phe Ala Cys Asp Ile Asn Pro Asp Ser Leu Lys Leu Leu Arg Glu Ser Ile Lys Leu Asn Asn Ile Asn Lys Lys Asn Ile Tyr Ile Ile Lys Gln Asn Ser Phe Met Leu Ser Lys Asn Val Gln Met Val Arg Lys Cys His Arg Ile Ile Leu Gly Leu Leu Pro His Ser Gln Pro Ala Trp Lys Asn Ala Phe Phe Leu Leu Asp Asn Lys Tyr Gly Gly Ile Leu His Ile His Gly Ile Gly Gln His Ile Phe Asp Glu Gln Val Cys Phe Ser Ser Ile Asn Thr Tyr Asp Tyr Ile Leu Lys Lys Lys Asp Val Asn Ile Ser

1785 1775 1780 Ser Ile Asn Lys Leu Thr Lys Leu Gln Met Val Glu Glu Tyr Val 1795 1800 Ser Asn Val Glu Asp Ser Asn Tyr Val Glu Glu Ile Lys Lys Asn 1805 1810 Lys Asp His Phe His Asn Lys Tyr Ile Asn His Tyr Asn Ser Asn 1830 1820 1825 Tyr Asn Lys Lys Leu Tyr Leu Gly Asn Asn Ile Pro His Asn Leu 1845 1835 1840

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Tyr Asp Asn Leu Lys Asn Asn Ile Phe Trp Asn Ile Ala Ile Ser 1865 1870 1875

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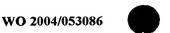
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Leu Glu Tyr Phe Tyr Ser Lys Leu Asn Ser Asn Ile Phe Asp Ile Phe 65 70 75 80



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Ala Phe Asn Lys Tyr Tyr Val Ser Asn Val Asn Thr Asp Asn Lys Glu 225 230 235 240

Asn Asn Val Asn Ile Asn Gln Glu Lys Lys Asn Ile Phe Val Asp Asn 245 250 255

Asp Lys Asn Ile Asn Gly Asp His Tyr Asp Asp Asp Val Glu Asn Ile 260 265 270

Glu Lys Lys Asn Tyr Lys Glu Tyr Ile Tyr Lys Lys Asn Ile Tyr 275 280 285

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Leu Leu Leu Asn Asn Ile Leu Arg Asp Ile Lys Cys Val Phe Phe 305 310 315 320

Asn Leu Glu Ser Glu Lys Asn Thr Ile Asn Ala Phe Ser Ile Asn Tyr

12

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Leu Leu Phe Asp Asn Val Tyr Tyr Glu Lys Lys Glu Asn Ser Asn Arg 355 360 365

Glu Glu Ile Asn Asp Lys Val Ser Lys Gln Gly Cys Asn Leu Asn Asp 370 380

Ser Asp Ser Ser Asn Val Leu Tyr Ile Asn Ile Gln Asn Ile Lys Asp 385 390 395 400

Tyr Asp Ile Leu Tyr Lys Glu Asp Asn Lys Asn Tyr Asn Asp Val Glu 405 410 415

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Asp Leu Lys Asn Met Ala Leu His Ile Phe Phe Tyr Lys Ile Ile Asp 435 440 445

Glu Thr Glu His Val Val His Met Asn Lys Lys Glu Tyr Lys Tyr Phe 450 455 460

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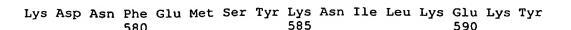
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Asn Ser Ser Ile Ile Gln Asn Leu Ile Asn Phe Leu Cys Gln Lys Ile 545 550 560

Ser Gln Asp Val Phe Ile Ile Glu Tyr Asp Asp Met Pro Phe Glu Asp 565 570 575



Glu Cys Leu Phe Pro Ile Asp Leu Ser Phe Leu Arg Asp Asp Ile Asn 595 600 605

Met Leu Cys Lys Arg Gly Asp Ala Thr Asn Asp Asp Asn Glu Asp Asn 610 615 620

Ile Ile Asn Ser Asn Asp Asp Arg Leu Glu Val Val Ser Lys Lys 625 630 635 640

Glu Val Asn Asp Asp Asn Lys Asn Ile Val Thr Ile Asn Leu Ile Arg 645 650 655

Ile Lys Asn Glu Leu Val Glu Thr Phe Phe Tyr Leu Asn Asp Ile Ser 660 665 670

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Ser Glu Arg Glu Asn Val Val Asp Ile Phe Asn Ser Tyr Met Lys Leu 725 730 735

Ser Ser Leu Ser Arg Asn Leu Pro Phe Ala Asn Gln Lys Asp Asp Lys 740 745 750

Tyr Lys Leu Arg Arg Gln Gln Lys Asp Glu Arg Arg Lys Ala Ile Ile 755 760 765

Ala Lys Tyr Phe Tyr Ile Ser Ser Leu His His Pro Ile Val Ile Ser 770 775 780

Glu Asn His Pro Trp Ile Lys Tyr Tyr Ser Tyr Asn Ile Glu Lys Leu 785 790 795 800

Tyr Asp Tyr Leu Arg Asn Glu Glu Lys Lys Gly Ile Thr Gln Arg 805 810 815

Met Lys Val Leu Phe Asp Ser Ser Ser Glu Arg Glu Asp Asp Glu Lys 820 825 830

Asp Gly Asp His Glu Ile Val Lys Ile Ser Asn Ile Ser Ser Asp Leu 835 840 845

Lys Asn Lys Asn Lys Asn Lys Arg Leu Ser Asp Ser Lys His Thr 850 855 860

Asn Glu Lys Thr Ile Met Lys Lys Leu Cys Thr Asn Ile Lys Leu 865 870 875 880

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Ile	Tyr 1295	His	Glu	Val	Asn	Gly 1300	Arg	Phe	Ser	Thr	Lys 1305	Gly	Tyr	Ser
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Phe	Leu 1400	Ala	Leu	Ser	Ala	Thr 1405	Ile	Gly	Asn	Ile	Asn 1410	Cys	Phe	Tyr
Ser	Trp 1415		Gln	Asn	Val	Leu 1420	Leu	Lys	Lys	Gly	Arg 1425	Ser	Ile	Asn
	Leu 1430										Ser 1440		Leu	Ile
Leu	Tyr 1445		Tyr	Thr	Asn	Lys 1450	Asn	Leu	His	His	Leu 1455	Asn	Pro	Leu
Thr	Cys 1460		Asn	Phe	Arg	Asp 1465	Ile	Leu	Tyr	Lys	Gly 1470	Ile	Asn	Lys
Asp	Phe 1475		Cys	Asn	Pro	Arg 1480	Glu	Ile	Tyr	Glu	Ile 1485	Ile	Ile	Ile
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Val	Tyr 1535	Leu	Ile	Gln	Asn	Asn 1540	Tyr	Ile	Asn	Asn	Leu 1545	Glu	Tyr	Asp
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Asn	Asn 1595	Val	Asp	Asp	Glu	Asp 1600	Val	Lys	Thr	Asn	Asp 1605	Lys	Val	Ile
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Gln	His 1715		Lys	Tyr	Tyr	Gly 1720		Glu	Glu	Arg	Ala 1725	Phe	Asn	Thr
Lys	Met 1730		Asn	Lys	Met	Arg 1735	_	Glu	Lys	Tyr	Glu 1740	Asn	Met	Leu



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Gln	Arg 1760	Leu	Glu	Gln	Asn	Ile 17 <b>6</b> 5	Asp	Lys	Glu	Tyr	Leu 1770	Asp	Met	Leu
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Tyr	Asp 1790		Asp	Phe	Туг	Phe 1795		Asn	Gln	Lys	Val 1800	Tyr	Cys	Asn
Tyr	Val 1805	Thr	Glu	Ile	Glu	Asp 1810	Leu	Ile	Lys	Asp	Ala 1815	Gln	Lys	Ala
Ile	Glu 1820		Arg	Lys	Tyr	Lys 1825		Ile	Leu	Ile	Glu 1830	Gly	Leu	Arg
Arg	Gly 1835		Gly	Leu	His	Tyr 1840	Glu	Val	Leu	Pro	Tyr 1845	Lys	Phe	Thr
Ile	Ile 1850		Glu	Ser	Leu	Phe 1855		Leu	Gly	Phe	Val 1860	Lys	Ile	Ile
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Tyr	Gly 1910		Ile	Ile	Ile	Trp 1915		Ile	Asn	Phe	Lys 1920	Asn	Leu	Lys
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Leu	Lys 1955		Ile	Arg	Glu	Asn 1960		Glu	Gly	Ser	Leu 1965		Asn	Lys

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Cys Gly Asn Gly Ile Gln Val Arg Ile Lys Pro Gly Ser Ala Asn Lys 340 345 350

Pro Lys Asp Glu Leu Asp Tyr Ala Asn Asp Ile Glu Lys Lys Ile Cys 355 360 365

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Lys Asn Asn Lys Ser Thr His Thr Tyr Lys Lys Asn Asn His Ile
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Asn Lys Met Gln Ser Ser Phe Phe Met Asn Arg Phe Tyr Ile Thr Thr 305 310 315 320

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Lys Val Leu Lys Glu Asn His Glu Gln Lys Leu Ser Glu Tyr Tyr Asp 340 345 350

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Thr Asn Asp Phe Ile His Ser Asp Asn Ser Leu Lys Glu Thr Asp Gln
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Leu Phe Asn Lys Glu Thr Leu Arg Ser Lys Lys Gly Ser Asn Glu 340 345 350

Asn Ile Ser Lys Glu Lys Leu Asn Glu Leu Leu Glu Lys Tyr Lys Ile 355 360 365

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Glu Lys Gln Asn Ile Pro Ile Tyr Ile Tyr Ile Lys Asn Lys Glu Tyr 385 390 395 400

Asp Ile Lys Asp Val Ile Leu Leu Leu Asp Asp Tyr His Phe Glu Thr 405 410 415

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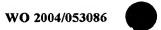
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Ile Val Phe Ser Lys Ile Gln Arg Lys Ile Lys Thr Asn Ile Phe Phe 500 505 510

Lys Lys Lys Lys Ile Leu Gln Asp Tyr Val Ile Leu Asn Glu Asp 515 520 525



Asn Ala Asn Arg Lys Ile Asp Val Tyr Ile Tyr Arg Arg Ile Leu Lys 530 535 Ser Val Asp Met Phe Ser Ser Ile Phe Glu Asn Tyr Asn Asn Glu Asn 555 550 545 Ile Tyr Ile Ser Asn Ile His Phe Ala Val Leu Phe Leu Thr Leu Thr 565 570 Val Tyr Pro Ile Asn Asn Phe Ile Asp Asp Asn Asn Met Ser Asn Val 580 585 Val Glu Asn Lys Ile Leu Asn Pro Gln Lys Asn Leu Ile Ile Asn Asn 600 Asn Pro Phe Leu Asp Ile Asn Lys Asn Asn Ile Asn Asp Glu Lys Leu 610 Leu Tyr Lys Met Asn Tyr Leu Lys Gln Asp Ile Asn Asn Ile Asn Asn 635 Tyr Asn Gln Gln Lys His Pro Ile Ile Ser Phe Ile Ile Glu Ile Leu 650 Glu Leu Leu Phe Tyr Asn His Phe Tyr Thr Asn Asn Ala Asn Leu Leu 665 Asn Leu Lys Asp Tyr Gln Lys Tyr Asp Trp Val Phe Asn Met Asn Thr 675 680 Tyr Glu Asn Tyr His Asn Ile Glu Ala Cys Leu Lys Lys Leu Glu Val 700 Tyr Tyr Ser Phe Ser Ser Phe Glu Asp Val Ile Cys Glu Asn Asn Lys Gly Gly Lys Glu Phe Glu His Asn Glu Ile Asn Asn Glu Ile Val Asn 730 Asp Leu Gly Ile Phe Tyr Arg Lys Lys Glu Phe Lys Asn Ser Leu Ile

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Leu Leu Asn Leu Tyr Asn Ile Ile Met Glu Asn Thr Leu Glu Tyr Asn 765 760 765

Pro Ser Phe Phe Tyr Leu Ser Phe Lys Ile Leu Asn Thr Leu Leu Tyr 770 775 780

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Pro His Val Ser Glu Lys Glu Lys Gln Lys Ile Gln Thr Ile Asn Asn 805 810 815

Asn Ile Ser Asn Asn Met Tyr Asp Lys Phe Asp Leu Ser Phe Ile Ile 835 840 845

Phe Lys Asn Ile Phe Phe Phe Leu Lys Ile Tyr Ile Asp Asn Asp Ile 850 855 860

Asn Ile Tyr Ile Leu Ile Asn His Val Ile Ile Pro Ser Leu Phe Tyr 865 870 875 880

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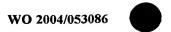
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Ser Ile Lys Lys Lys Met Lys Gln Gln Arg Lys Phe Asp Tyr Asn Glu 995 1000 1005



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Ala Ser Glu Ser Asn Phe Tyr Lys Tyr Lys Lys Arg Lys Asn Asn Thr 50 55 60

Tyr Glu Tyr Lys Asp Asp Lys Asp Tyr Thr Ser Tyr Asp Asn Lys Phe 65 . 70 75 80

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Leu Leu Ser Arg Phe Ile Phe Ile Tyr Lys Leu Val Asp Asn Ile Ser 100 105 110

Glu Asp Glu Ile Asp Glu Leu Ile Arg Asn Ile Ser Ile Asn Asn Ala 115 120 125

Phe Ser Leu Pro Val Asn Ile Tyr Ile Asn Lys Leu Ser Phe Phe Ser 130 135 140

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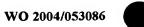
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Asp Asp Gln Asn Thr Asn Met Leu Ile Leu Lys Asn Met Asp Gly Asn 435 440 445

Ile Leu Ile Lys Asp Phe Ile Gln Phe Leu Asn Val Thr Phe Asp Lys 450 455 460

Asn Asp Val Ser Cys Ile Tyr Leu Phe Asn Asp Ile Lys Gly Ser Ser 465 470 475 480

Lys Lys Cly Phe Cys Phe Ile Glu Phe Tyr Asn Ile Asn Met Ala 485 490 495

Lys Lys Val Met Asn Asn Met Glu Lys Asn Tyr Tyr Leu Asn Phe Gln

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Ala Thr Val Val Lys Asn Asn Ile Pro Tyr Phe Asn Phe Phe Val Asn 545 550 555 560

Tyr Phe Glu Ala Val Val His Met Asn Ile His Cys Tyr Thr Tyr Phe 565 570 575

Leu Met Trp Ser Ser Gln Ile Ile Leu Lys Lys Gly Lys Pro Glu
580 585 590

Leu Ser Glu Phe Phe Phe Asp Tyr Asn Ser Gln Tyr Tyr His Pro 595 600 605

Leu Tyr Gln Leu Tyr Phe Asp Asn Asn Thr Lys Tyr Tyr Met Ser Leu 610 615 620

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Val Tyr Leu Asp Asn Leu Gly Glu Asn Val Tyr Glu Arg Glu Asn Tyr 645 650 655

Asp Lys Lys Phe Ser Leu Met Asp Ala Ser Lys Asn Lys Glu His Glu 660 665 670

Glu Thr His Gln Gln Ala Arg Ile Asn Asp Asp His Lys Tyr Asp Asn 675 680 685

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Asn Asn Leu Ser Ile Leu Glu Lys Lys Asn Lys Glu Ile Ile Lys Lys 755 760 765

His Phe Thr Thr Asp Ser Ala Asp Asp Glu Asp Glu Glu Asn Asp Asn 770 775 780

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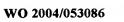
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Lys Lys Lys Lys Lys Ile Leu Ile Gln Ile Ile Gln Glu Tyr Asn 65 70 75 80

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Tyr Thr Asp His Thr Asn Gln Asn Ala Lys Ser Lys Ile Tyr Asn Tyr 115 120 125

Asp Met Asn Asp Asp Ser Tyr Ser Asn Tyr Val Asn Asn Asn Val 130 135 140

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Pro Leu Gln Phe Val Cys Glu Thr Glu Gly Arg Ser Arg Asn His Glu 165 170 175

His Tyr Pro Asp Val His Gly Asp Asn Ile Lys Tyr Asn Lys Cys Asp 180 185 190

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Lys Arg Lys Lys Met Asn Ser Asn Leu Cys Val Ile Asn Lys Ile Tyr 305 310 315 320

Lys Tyr Pro Ile Lys Tyr Cys Glu Leu Asn Ser Lys Ala Phe Val Phe 325 330 335

Phe Ile Ile Lys Asn Val Gly Val His Lys Ile Thr Tyr Tyr Ser Tyr 340 345 350

Asn Lys Leu Phe Ser Lys Asp Gly Val Leu Asn Gln Gly Ile Gln Ile 355 360 365

Cys Lys Leu Tyr His Val Asn Lys Asn Lys Lys Ile Lys Gln Ile Ile 370 375 380

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Glu Lys Cys Asn Lys Lys Leu Asn Met Glu Lys Thr Phe Gly Val His 435 440 445

Lys Ser Ser Arg Tyr Asn Tyr Lys Thr Tyr Lys Lys Lys Lys Lys Ile 450 455 460

Asp Met Cys Lys Asn Tyr Cys Asp Asp Ile Leu Asp Thr Tyr Asn Ser 465 470 475 480

Lys Tyr Tyr Lys Gly Glu Leu Ser Gly Gln His Lys His Ile Lys Met

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Phe Asn His Gly Lys Asp Glu Thr Phe Tyr Lys Glu Leu Tyr Lys Cys 515 520 525

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Tyr Asn Glu His Lys Lys Asp Met Ser Thr Leu His Asp Asn Leu Phe 740 745 750

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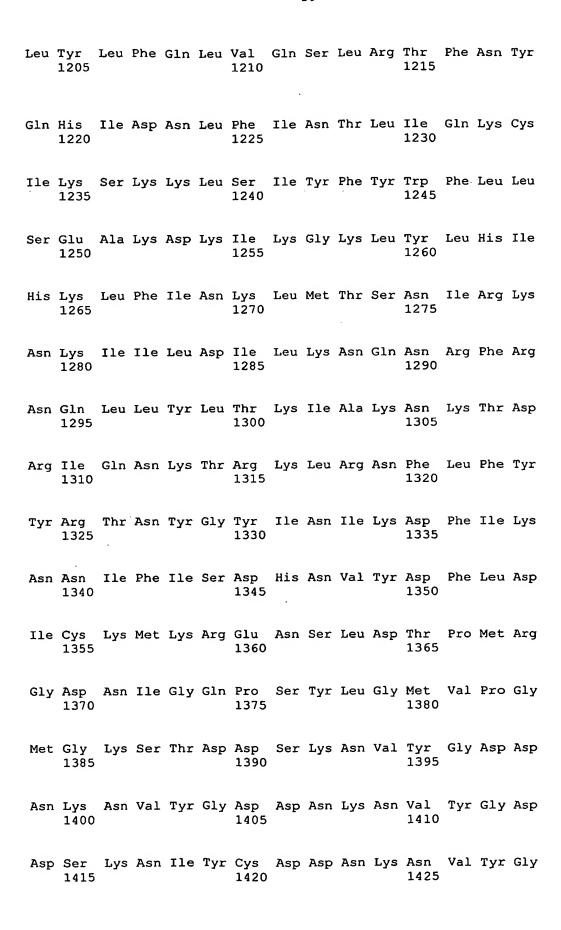
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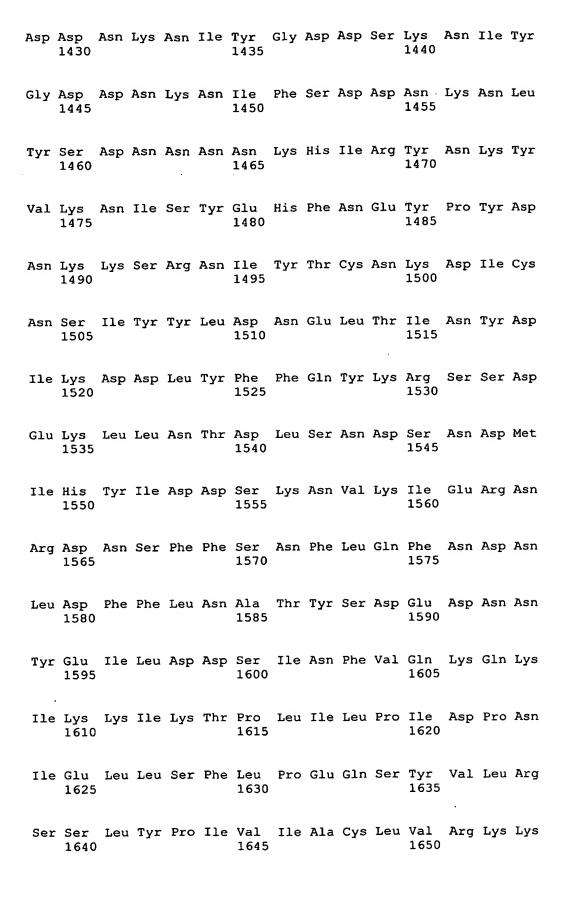
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Tyr Ile Ile Asp Ile Ile Lys Asn Ser Lys Lys Glu Glu Ile Lys 1190 1195 . 1200







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Asn	Leu 1685	Ser	Tyr	Asp	Lys	Ser 1690	Tyr	His	Ser		Tyr 1695	Asn	Ser	Gln
Phe	Ile 1700	Lys	Thr	Leu	Gln	Asn 1705	Ser	Phe	Glu	Ser	Thr 1710	Thr	Ser	Leu
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Arg	Lys 1865	_	Tyr	Asn	Glu	Ile 1870		Gln	Leu	Ser	Ile 1875	Lys	Lys	Tyr
Ile	Tyr	Lys	Ala	Gly	Asp	Asp	Leu	Arg	Gln	Asp	His	Leu	Val	Ile

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Asp Leu Lys Met Thr Leu Tyr Arg Val Leu Ala Leu Ser Thr Asp 1910 1915 1920

Asp Gly Phe Ile Glu Phe Val Asp Tyr Ala Glu Ser Ile Ser Ser 1925 1930 1935

Ile Lys Lys Asn Tyr Lys Gly Glu Ile Arg Gln Tyr Phe Ile Asp 1940 1945 1950

Asn Ser Thr Cys Ser Ser Ser Pro Leu Gly Phe Asp Thr Glu Ile 1955 1960 1965

Leu Gln Asn Phe Ile Ser Ser Cys Ala Gly Tyr Ser Val Ile Thr 1970 1975 1980

Tyr Ile Leu Gly Ile Gly Asp Arg His Leu Asp Asn Leu Met Val 1985 1990 1995

Thr Lys Asp Gly Arg Phe Phe His Ile Asp Phe Gly Tyr Ile Phe 2000 2005 2010

Gly Glu Asp Pro Lys Pro Phe Ser Pro Pro Met Lys Leu Cys Lys 2015 2020 2025

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Gln Phe Leu Lys Lys Cys Cys Leu Ala Tyr Lys Tyr Leu Arg Tyr 2045 2050 2055

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Tyr Val Glu Cys Ile Ile Glu Lys Ile Lys Lys Ile Lys Asn Glu Asn 115 120 125

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Ala Val Ser Ser Tyr Gln Thr Gly Thr Gln Thr Phe Asn Asn His Pro 145 150 155 160

Asn Phe Tyr Thr Asn Tyr Tyr Gln Ser Phe Ile Lys Asn Asp Asn Ile 165 170 175

Pro Tyr Ile Asn Gln Thr Asn Ile Phe Asp Asn Asn Ile Lys Asn Lys 180 185 190

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Leu Gly Val Lys Lys Glu Asp Thr Asp Asn Tyr Leu His Val Phe Ile 275 280 285

Leu Asn Asn Gly Asn Ile Tyr Gly Ser Gly Lys Lys Cys Ser Val Ser 290 295 300

Ile Ile Arg Lys Ile Gln Ile Asn Thr Asp Arg His Ile Thr Phe Lys 305 310 315 320

His Ile Ile Lys Thr Pro Leu Tyr Leu Tyr Lys Ser Lys Glu Asp Lys 325 330 335

Asn Lys Asn Asn Ser Asn Asn Asn Asn Asn Asn Asn Asn Ser Asn Asn 340 345 350

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Ser Asn Asn Asn Thr Thr Thr Asn Asn Ser Ser Ser Ser Asn Asn Ser 405 410 415

Asn Asn Asn Tyr Tyr His Asn Asn Tyr Lys Asn Glu Lys Glu Leu

Asn Asn Ser Ser Ser Leu Glu His Ser Ser Ile Ile Met Asn Asn Asp

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Leu 465	Asn	Asn	Met	Asn	Val 470	Asn	Gln	Ser	Asn	Met 475	Lys	Glu	Asn	Asn	Asn 480
Ile	Île	Asp	Туг	Met 485	Asn	Asn	Asn	Asn	Asn 490	Asn	Asp	Asn	Tyr	Ser 495	Asn
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Phe	Thr	Glu 515	Asp	Ser	Gln	Lys	Arg 520	Asn	Pro	Leu	Gln	Thr 525	Tyr	Asn	Thr
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Tyr 545	Asn	Phe	Pro	Asn	Ile 550	Asn	Asn	Met	Asp	Ser 555	Asn	Ile	Tyr	Asn	His 560
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Ile	Ser	Ile	Asn 580		His	Asn	Asn	Ile 585	Phe	Asn	Asn	Met	Asn 590	His	Leu
Asn	His	Leu 595	Asp	Asn	His	Ser	<b>Tyr</b> 600		Gln	Asn		Leu 605		Lys	Asn
His	Met 610		Val	Asn	Thr	Asn 615		Leu	Tyr	Asn	Asn 620	Pro	Ile	Met	Asn
Asn 625		Asn	Asn	Asp	Gln 630	Ile	Asn	Asn	Leu	Ser 635	Ile	Pro	Asn	Asn	Lys 640
Asn	Glu	Asp	Asn	Asn 645		Ile	Asn	His	Asp 650		Ser	Asn	Asp	Asp 655	
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Tyr	Phe	Ala 675	Leu	Asn	Pro	Lys	Туг 680		Asn	His	Gln	Asn 685	His	Asn	Ile

Asn Asn Ile Gln Asn Asn Leu Asn Glu Gln Ile Lys Glu Lys Asn 690 695 700

Asp Gln Gln Asn His Asn Ile Lys Glu Ile Lys Asn Lys Glu Leu Leu 705 710 715 720

Asn Asp Thr Ile Ser Ser Ile Glu Asp Thr Asn Asp Asn Ser Tyr Ser 725 730 735

Lys Tyr Ile Thr Ser Ser Asp Ile Ser Gln Asn Asn Thr Leu Asn Ser 740 745 750

Phe Gln His Asn Lys Glu Ile Ser Val Asn Phe Met Tyr Asn Asn Ile 755 760 765

Ile Leu Asp Asn Asn Asn Ile Asn Asp Asp Asn Asn Asn Asn Asn 770 775 780

Asn Tyr Phe Cys Ile Pro Cys Gly Tyr Asn Thr Lys Glu Tyr Lys Tyr 785 790 795 800

Asn Ile Tyr Asn Thr Tyr Asn Tyr Pro Asn Asn Ala Asn His Ile Tyr 805 810 815

Asn Asn Met Asn Ile Ser Tyr Asn Asn Ser Ala Tyr Asn Asn Asn Tyr 820 825 830

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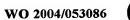
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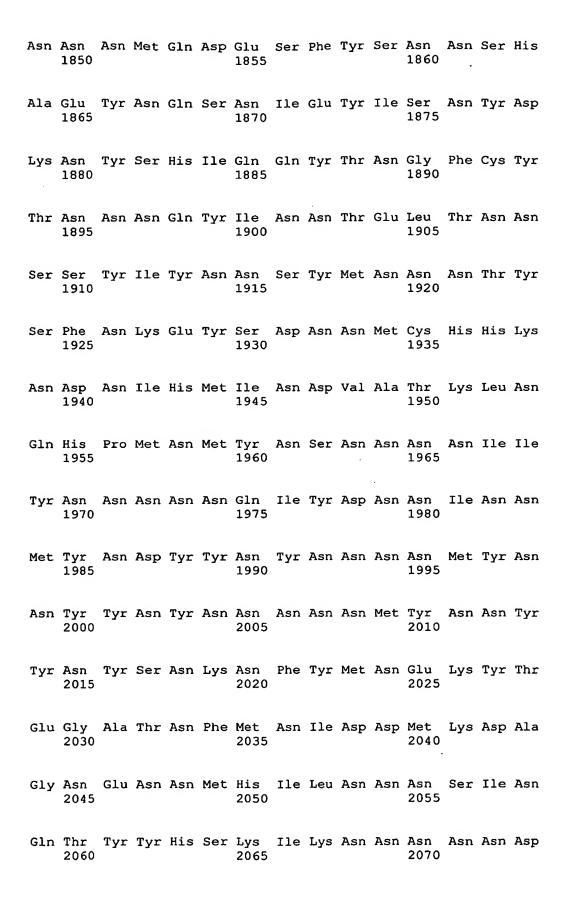


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- Ile Pro Leu Asp Asn Asn Thr Tyr Asn Ser Asn Lys Asn Lys Ile Ile 980 985 990
- Tyr Lys His Ile Ile Asn Asp His Ile Asn Gln Lys Asp Asn Asn Val 995 1000 1005
- Glu Tyr Glu Asn Leu Asn Asn Ser Cys Asp Asn Thr Gln Asn Lys 1010 1015 1020
- Glu Thr Phe Cys Asn Gln Asp Leu Ile Asn Ser Ser Asn Ile Asn 1025 1030 1035
- Asn Asn Ile Ser Ser Tyr Thr Phe Gln Asn Asn Asn Asp Phe Tyr 1040 1045 1050
- Thr Lys Lys Lys Ser Met Gln Tyr Asn His Asp Asn Ile Tyr Lys 1055 1060 1065
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- Gln Asn Val Ala Gln Asn Val Ala Gln Asn Val Glu Gln Asn Val 1130 1135 1140
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- Asn Asp Ile Val Ile Cys Asn Asn His Asn Asn Ser Ser His Val 1265 1270 1275
- Gln Lys Asn Tyr Tyr Asn Met Asn Glu Ser Met Ile Asn Glu Asn 1280 1285 1290
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Gln Tyr Lys Ser Asp Asn Ile Leu Ser Cys Glu Lys Asn Phe Ile 1625 1630 1635 Thr Leu Lys Asn Asn Asn His Asn Asn His Asn Asn Asn Asn 1640 1650 1645 Tyr Tyr Tyr Tyr Ile Asn Asn Asp Asn Ile His Leu Asn Asn 1655 1660 1665 1660 Ser His Ile Asp Ile Met Lys Thr Asn Asn Ile Asn Lys Asp Met 1670 1675 Thr Thr Asn Ser Thr Pro His Phe Lys His Asn Ile Ile Ser Asn 1685 1690 1695 Asp Cys Ser Pro Asn Asn Ile Asn Gln Asn Ile Phe Val Asp Pro 1700 1705 1710 Asn Lys Tyr Ile Tyr Asn Asn Ile His Thr Asn Tyr Asn Ala Tyr 1720 1725 1715 His Glu Glu Ser Leu Gln Val Val Gly Asn His Asn Ser Ser Ser 1735 . 1740 1730 Leu Leu Arg Asn Ile Asn Glu Ser Phe Ser Asn Gln Tyr Asp Asn 1750 17.45 Lys Lys Asn Leu Glu Ala His His Ile Asp Asp Asp Lys Asn Lys 1765 1770 1760 Glu Ala Phe His Asn Asp Asp Lys Asn Lys Glu Ala Phe His 1780 Asn Val Asp Asp Lys Asn Lys Glu Thr Phe His Asn Asp Asp Asp 1795 1800 Lys Asn Lys Glu Ala Leu His Asn Asp Asp Lys Asn Lys Glu 1810 Ala Leu His Asn Asp Asp Asp Lys Asn Val Glu Ala Tyr His Asn 1825 1820 Asp Asn Tyr Asn Asp Asn Tyr Asn Asn Asn Tyr Tyr Phe Asp Gly 1845 1840 1835



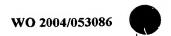
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Lys Asp Asn Val Asn Asn Val Glu Gly Val Leu Gly Ile Lys Lys Asp Lys Glu Asn Asp Asn Asn Glu Glu Glu Asn Asp Glu Glu Glu Asn Asn Glu Glu Glu Asn Lys Glu Ala Gln Asn Asn Glu Glu Glu Asn Asn Asn Gly Asp Asn Asn Gly Asp Asn Asn Asn Asn Gly Asp Asn Asn Asn Asn Ile Phe Tyr Asn Met Glu Gly Ser Gln Lys Ile Cys His Asp Asp Ile Thr Leu Asn Glu Cys Leu Asn Ser Ile Asp Ile Asn Glu Gly Glu Lys Lys Thr Phe Glu Glu Asn Lys Ser Ser Phe Ser Met Leu Tyr Leu Phe Gly Lys Val Lys Phe Tyr Ile Ser Ile Ile Asp Ile Ile His Asn Lys Thr Asn Ser His Asp Leu Leu Trp Val Pro Arg Cys Cys Asn Gly Ser Tyr Gly Thr Phe Leu Lys Tyr Asn Tyr Ser Asn Met Asn Glu Ile Asn Lys Tyr Thr His Asp Glu Gly Ile Asp Ile Asp Ser Ile Asn Leu Lys Leu Met Glu Thr Arg Phe Ser Lys Asn Val Ala Ser Ser Arg 



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Asp	Asn 2615	Asn	Asn	Lys	Asn	Lys 2620	Asn	Asn	Asp	Asp	Asp 2625	Asn	Asn	Asn
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Ile	Glu 2720		Ile	Asn	Ser	Met 2725		Ser	Ile	Lys	Ser 2730		Asp	Gly
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Thr	Glu	Ser	Ile	Asn	Asn	Ile	Glu	Ile	Thr	Gln	Asn	Met	Asn	Thr



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Ile	Asn 2780	Asn	Val	Asn	Gly	Ile 2785	Asn	His	Thr	Asn	Gly 2790	Ile	Asn	His
Thr	Asn 2795	Gly	Ïle	Asn	Asn	Ile 2800	Asn	Thr	Met	Asn	Asn 2805	Met	Asn	Asn
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Ile	Asn 2885		Thr	Asp	Ile	Asn 2890	_	Asn	Asn	Met	Ile 2895	Ser	His	Asn
Asp	His 2900		Asn	Asn		Leu 2905		Ser			Asn 2910		Asn	Tyr
Tyr	Tyr 2915		Arg	Ala	Asn	Asn 2920		Ile	Pro	Asn	Asn 2925	Asn	Ser	Asn
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Ser	Gln 2975		Leu	Glu	Gly	Asn 2980	Thr	Asn	Phe	Ile	Asn 2985	Ile	Ser	Asn

Thr Phe Ile Asn Thr Asn Tyr Ser Asn Asp Phe His Gln Thr Asn 2995 2990

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Val Ala Ile Ile Leu Tyr Val Ile Phe Leu Val Leu Leu Phe Ile Tyr 55 50

Lys Ala Tyr Lys Asn Lys Arg Lys Leu Tyr Thr Asn Phe Phe Met Lys 65

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Thr Ala Leu Glu Arg Leu Leu Ser Leu Lys Lys Thr Ile Phe His Asp 50 55 60

Asn Arg Leu Val Thr Leu Cys Pro Val Glu Asn Asn Ile Thr Pro Ile 65 70 75 80

Glu Leu Glu Ala Ser Ile Ser Gly Lys Tyr Asp Ile Lys Val Tyr Arg 85 90 95

His Cys Glu Tyr Ile Leu Cys Ile Glu Gly Glu Gln Lys Ile Leu Ile 100 105 110

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Leu Pro Leu Leu Pro Lys Thr Trp Lys Pro Thr Ile Phe Leu Leu Asn 130 135 140

Glu Ser Asn Ile Phe Leu Arg Phe Ile Pro Asp Lys Cys Leu Val Ile 145 150 155 160

Ser Gln Val Ser Asn Ser Asp Ser Tyr Lys Val Asn Cys Ile Asn Phe 165 170 175

Ser Glu Gly Phe Cys Cys Cys His Pro Ile Asn Asn Leu Ala Leu Leu 180 185 190

Tyr Gly Glu Tyr Gln Gln Asn Gln Glu Ser Lys Ile Met Lys Leu Pro 195 200 205

Lys Leu Pro Ile Ser Asn Gly Lys Tyr Asn Tyr Phe Ile His Phe Phe 210 215 220

Thr Trp Gly Thr Met Phe Val Pro Lys Tyr Phe Glu Leu Ser Arg Gly 225 230 235 240

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Pro Lys Ile His Ile Ser Ile Glu Leu His Ser Ser Ser Pro Val Val 260 265 270

Cys Ser Met Glu Tyr Lys Lys Asp Phe Leu Ile Thr Ala Arg Lys Pro 275 280 285

Asn Ile Thr Asp Ile Glu Ile Tyr Thr Ile Ile Gln Asp Gln Leu Ile 290 295 300

Lys Tyr Asp Phe Ser Tyr Asp Leu Arg Leu Asn Lys Glu Asn Ala Ser 305 310 315

Ile Ser His Leu Asn Ile Pro Ile Gly Phe Lys Ile Cys Asn Glu Glu 325 330 335

Lys Glu Lys Lys Lys Asn Ser Ser His Ile Cys Lys Trp Thr Phe 340 345 350

Ile Glu Thr Lys Asp Gln Arg Thr Leu Asn Arg Ser Gly Asn Ser Ser 355 360 365

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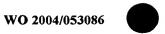
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Leu Lys Asn Glu Leu Asn Glu Gln Leu Ile Tyr Thr Tyr Tyr Asn Asn 65 70 75 80



Phe Asn Asn Asn Tyr Glu Tyr Tyr Asn Lys Ser Thr Glu Lys Leu Lys 85 90 95

Glu Lys Asn Asn Glu Asp Glu Tyr Asn Glu Glu Glu Glu Tyr Glu Pro 100 105 110

Thr Ala Asn Leu Gln Asp Lys Asn Lys Ile Asn Asp Met Asn Asn 115 120 125

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Ser Ser Ile Phe Ile Ser Phe Tyr Leu Ile Asn Lys His Trp Gln Arg 260 265 270

Ala Leu Lys Ile Ser Gln Leu Gln Lys Lys Ile Asn Ser Asn Phe Leu 275 280 285

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Lys His Ile Ser Ile Asn Ile Asn Arg Lys Cys Ala Ser Tyr Asn Asn 50 55 60

Ile Tyr Tyr Ile Asn Asn Asp His Pro Gly Leu Gly Lys Asn Ile Ser 65 70 75 80

Tyr Tyr Gln Asn Lys Asp Asn Met Gln Leu Lys His Phe Phe Asn Ser 85 90 95

Asn Lys Ile Asn Ile His Asp Asn Lys Ile Lys Thr Thr Gln Ser Tyr 100 105 110

Ser Tyr Tyr Glu Pro Leu Arg Tyr Pro Ala Phe Lys Met Ser Asp Lys 115 120 125

Ile Lys Ser Glu Thr Asn Glu Leu Lys Lys Met Asp Thr Lys Lys Asp 130 135 140

Val His Met Lys Asp Ile His Pro Lys Asn His Lys Ile Ser Lys Asn 145 150 155 160

Asp Asp Leu Gly Asn Asn Asn Ile Asp Asn Asn Asn Asn Asn Asp Asp 165 170 175

Asn Asn Asn Ser Asn Asn Asn Asn Asn Asn Ile Lys Cys Val Ser 180 185 190

Asn Arg Ser Thr Ser Asn Lys His Ile Asn Arg Arg Asn Met Cys Ile 195 200 205

Phe His Asn Lys Ile Asn Lys Lys Glu Lys Asn Ile Asn Glu Gln Gly 210 215 220

Glu Lys Asn Glu His Ser Lys Ile Asp His Lys His Phe Gly Asn His 225 230 235 240

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Gly Asn Ser Asn Asn Leu Glu His Glu His Val Gln Glu Lys Pro Ala 275 280 285

Arg Phe His Lys Lys Lys Arg Lys Lys Gln Asn Lys Leu Ala Gly 290 295 300

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Val Ile Glu Met Glu Lys Val Asn Tyr Leu Asp Asp Lys Val Asn Gly 325 330 335

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Ile Pro Lys Glu Val Met Tyr Ile Pro Ile Glu Glu Arg Cys Lys Ser 450 460



Ile Val Ser Ser Ser Asp Glu Glu Asn Leu Tyr Tyr Glu Lys Pro Tyr 470 465 Glu Glu Val Glu Asn Tyr Phe Glu Phe Ile Glu Asn Lys Asn Leu Ile 490 485 Asn Pro Ser Asp Ile Thr Asn Glu Val Lys Phe Ile Leu His Met Thr 500 505 Leu Leu Thr Leu Tyr Lys Asp Gln Ile Lys Pro Ser Tyr Gly Lys Ile 520 525 515 Lys Lys Arg Leu Thr Cys Phe Asn Glu Asn Leu Glu Ile Lys Tyr Asn 530 535 Phe Leu Asn Ile Tyr Ala Ser Leu Arg Asn Glu Tyr Ile Val Val Arg 550 Thr Lys Arg Asn Asn Ile Phe Val Leu Leu Arg Glu Thr Pro Lys Trp 565 570 Phe Leu Gly Trp Val Lys Thr Arg Cys Phe Lys Asn Ser Tyr Pro Lys 580 Lys Val Trp Lys Lys Leu Ile Glu Tyr Phe Leu Asn Met Thr Lys Ser 595 Asn Met Asn Asn Asn Leu Tyr Val Ser Met Tyr Ile Pro Phe Ile Lys 615 Lys Phe Tyr Asp Lys Arg Phe Ile Phe Tyr Leu Asn Glu Lys Asp Asn 630 Glu Lys Asn Lys Cys Tyr Glu Lys Ile Tyr Asn Phe Ser Phe Leu Ser 650 Phe Asp Met Asn Glu Gln Lys Lys Lys Arg Asn Asn Phe Asn Val Leu Phe Tyr Ile Tyr Asn Met Tyr His Asn Asn Phe Ser Tyr Phe Ser Gln 680 Cys Asn Asp Tyr Tyr Ile Lys Asn Val Glu Lys Asn Phe Leu Leu Tyr 695 690



Tyr Thr Tyr Ile Phe Phe Asn Tyr Asp Lys Asn Asp Leu Asn Asn Asn 705 710 715 720

Asn Ser Asn Ile Asp Leu Ser Lys Lys Asn Tyr Leu Cys Glu Asp Lys 725 730 735

Ser Ser Cys Ser Asn Asn Asn Ser Ser Ser Ser Ser Ser Tyr
770 775 780

Asn Asn Asn Cys Asn Asn Tyr Thr Ser Leu Tyr Val Glu His Leu Phe 785 790 795 800

Asn Asp Lys Lys Glu Asn Ile Leu Gln Thr Asp Glu Ile Ile Lys Tyr 805 810 815

Asp Ile Thr Lys Asn Leu Ile Asn Glu Glu Asn Asn Ile Asp Thr Thr 820 825 830

Asn Met Phe Asp Ile Phe Asn Asn Asp Ile Tyr Glu Val Ala Asp Ile 835 840 845

Leu Lys Lys Lys Asn Phe Pro Ile Leu Lys Asp Tyr Ser Leu Gly Lys 850 860

Ile Ala His Ile Ile Tyr Leu Cys Leu Tyr Asn Gly Leu Leu Glu 865 870 875 880

Glu Asn Gln Lys Ile Ile Pro Ala Cys Ser Ser Lys Asn Ile Ile Ser 885 890 895

Ser Ile Phe Tyr Ile Lys Asn Lys Asn Ser Tyr Leu Tyr Asp Asn Tyr 900 905 910

Ser His Leu Asn Gln Asn Phe Tyr Cys Asp Asn Asn Ile Ser Thr 915 920 925

Tyr Gly Tyr Asp Tyr Asn Glu Ser Thr Ser Ile Asn Leu Met Thr Lys 930 935 940

Glu Tyr Asp Asp Lys Met Asp Ser Phe Leu Asn Val Tyr Glu Asn Phe 945 950 955 960

Leu Lys Asn Glu Glu Gly Leu Phe Phe Ser Lys Lys Asn Asn Lys 965 970 975

Cys Asp Val Asn Val Ser Leu Asn Lys Cys Thr Glu Glu Phe His Ile 980 985 990

Pro Ala Ile Thr Asn Leu Glu Glu Ala Lys Phe Lys Ile Glu Arg Leu 995 1000 1005

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Glu Asn Asn Asn Asn Lys Phe Asn Asn Ser Ser Leu Glu Val Cys 1115 1120 1125

Thr Ile Met Lys Asp Asn Ala Lys Lys Lys Asn Ser Phe Phe Ile 1130 1135 1140

Thr Tyr Ser Tyr Trp Lys Tyr Met Ser Lys Lys Glu Lys Gln Asn 1145 1150 1155

Asp Ile Leu Asp Asn Val Ser Phe Leu Lys Gly Glu Gln Asn Tyr 1160 1165 1170 Ile Phe Ser Asp Asp Ile Trp Lys Ile Asn Lys Cys Ser Phe Asp 1175 1180

Lys Thr Asn Pro Ile Gln Gln Ser Gly Lys Asp Ile Pro Leu Tyr 1195 1200

Tyr Lys Asn Met Lys Lys Ile Asn Thr Gly Ile Phe Asn Met Pro 1205 1210 1215

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Asp Ser Leu Val Leu His Ala Lys Glu Arg Glu Val Gly Tyr Phe Lys

Arg Ile Phe Lys Leu Pro Asn Asn Ile Leu Asp Asp Thr Ala Lys Ala

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Phe Leu Gln Ile 100

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Phe Asn Cys Asp Ile Ala Asn Lys Ala Val Gln Arg Glu Asp Glu Glu 35 40 45

Ser Met Gly Val Phe Cys Leu Lys Glu Lys Val Lys Asn Lys Ile Asn 50 55 60

Lys Lys Tyr Asn Lys Lys Asn Lys Asp Asn Ile Phe Lys Asn Asp Asn 65 70 75 80

Asn Thr Phe Ser Val Cys Glu Tyr Thr Glu Leu Asn Glu Cys Ile Leu 85 90 95

Asn Asn Lys Glu Leu Phe Lys Tyr Gly Asn Ile Cys His His Ile Ile 100 105 110

Thr Val Asp Phe Leu Lys His Ile Val Lys Asn Arg Ile Tyr Asn Lys 115 120 125

Leu Lys Leu His Lys Ile Ile Arg Lys Lys Gln Tyr Thr Asp Ile Pro 130 135 140

Ser Leu Ile Asn Asp Asn Asn Glu His Leu Ile Asn Ser Lys Val Phe 145 150 155 160

Cys Tyr Glu Tyr Phe Ile Phe Asp Ile Phe Lys Tyr Ala Arg Asn Ile 165 170 175

Leu Ser Leu Glu Val Asn Arg Gln Lys Glu Phe Tyr Pro Ile Lys Asn 180 185 190

Lys Asn Asn Glu Tyr Gly Ile Leu Asn Ala Gln Lys Ala Leu Ser Asn 195 200 205

Leu His Lys Ser Trp Leu Gln Tyr Lys Asn Ile Asn Ile Ile Asp Asn 210 215 220

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35 40 45

Ser Val Leu Pro Glu Val Glu Asn Val Ile Glu Arg Lys Asp Ile Tyr 50 55 60

Arg Gln Ile Asn Phe Met Glu Thr Phe Val Ser Ser Asn Asn Met Met 65 70 75 80

His Asp Arg Glu Lys His Thr Ser Asn Asp Ser Gly Ser Tyr Glu Ile 85 90 95

Thr Gly Ile Val Asp Gly Met Lys Ile Gly His Pro Ile Ser Val Ala 100 105 110

Leu Gly Ser Gln Tyr Ser Asn Tyr Phe Asp Tyr Leu Gln Ile Val His 115 120 125

Leu Asp Tyr Thr Asn Ser Arg Phe Ser Phe Thr Val Gly Glu Gly Lys
130 135 140

Tyr Tyr Leu Arg Thr Tyr Gly Ser Thr Tyr Met Thr Pro Ser Ala Ile 145 150 155 160

Lys Ile Lys Val Pro Cys Glu Lys Cys Lys Phe Ile Asn Ser Glu Tyr 165 170 175

Ser Gly Ile Ile Lys Ile Ile Pro Tyr Glu Thr Asn Asn Asn Leu Phe 180 185 190

Ile Tyr Asn Trp Val Leu Gln Thr Ser Ser Pro Leu Ala Leu Glu Asn 195 200 205

Ile Asn Thr Val Phe Ser Asp Glu Ala Asp Leu Ile His Gly Asn Ser 210 215 220

Leu Ser Glu Glu Phe Lys Ile Asp Ser Ser Ala Ala Ala Thr Ser Leu 225 230 235 240

Asn Thr Phe Tyr Gly Ile Val Leu His Gly Ile Trp Ser Ser Glu Tyr 245 250 255

Ala Glu Arg Leu Leu Thr Val Ile Ser Glu Phe Pro Asp Cys Val Lys 260 265 270

Met Ser Ala His Asp Lys Asn Ala Arg Ser Lys Gln Arg Lys Asn Gln 275 280 285

Lys Trp Ile Leu Val Asn Glu Asp Leu Gly Ser Phe Asp Met Lys Met 290 295 300

Glu Val Cys Glu Glu Val Asn Cys Asp Tyr Ser Ala Ile Ile His Val 305 310 315 320

Ser Lys His Ala Phe Glu Tyr Ser Lys Leu Val His Asn Arg Gly 325 330 335

Arg Asn Gly Arg Tyr Tyr Ser Arg Arg Val Glu Lys Ile Leu Ile Arg 340 345 350

Ala Leu Leu Ser Leu Asp Phe Ser Leu Phe Ile Thr Tyr Phe Gln Gln 355 360 365

Lys His Gly Val Thr Leu Leu Asp Pro Gln Tyr Asp Tyr Glu Leu Ile 370 375 380

Thr Asn Met Ser Gly Tyr Ser Ser Asn Asn Tyr Gln Ser Trp Asn His 385 390 395 400

Asn Leu Glu Glu Leu Val Glu Leu Ala Thr Ser Trp Asp Glu Tyr Pro 405 410 415

Lys Gly Leu Gln Lys Val Gln Gly Leu Ser Tyr Leu Leu Arg Arg Lys
420 425 430

Asn Gly Thr Lys His Pro Val Tyr Pro Thr Ala Pro Ala Val Ala Phe 435 440 445



Pro Ala Gly Ser Gln Asn Asn Ser Phe Ile Glu Phe Met Glu Ser Ala 450 455 460

Phe Val Asn Tyr Val Asp Ile Ser His Leu Val Ile His Glu Val Ala 465 470 475 480

His Phe Ile Trp Val Asn Thr Val Ser Lys Glu Leu Lys Glu Lys Trp
485 490 495

Ile Gln Ile Gly Gln Trp Tyr Lys Glu Pro Leu Ser Pro Ser Glu Trp 500 505 510

Ala Thr Lys Leu Glu Val Glu Phe Val Ser Ala Tyr Ala His Asp Lys 515 520 525

Asn Pro Ala Glu Asp Phe Ala Glu Ser Met Ala Thr Tyr Val Leu Asn 530 535 540

Ser Lys Leu Leu Asn Ser Arg Ser Phe Asp Lys Phe Lys Trp Ile Gln 545 550 555 560

Asp Asn Leu Phe Gly Gly Gly Phe Tyr Ile Thr Thr Gly Thr His Lys 565 570 575

Phe Asp Val Ile Asn Leu Gly Asn Glu Val Tyr Tyr Phe Pro Gly Lys 580 585 590

Val Thr Arg Val Arg Ala Lys Val Leu Gly Ser Pro Thr Glu Asp Lys 595 600 605

Leu Val Lys Ile Tyr Ile Ser Leu Leu Ser Ser Asp Gly Ser Glu Gly 610 615 620

Cys Ala Lys His Gly Tyr Ala Arg Ile Phe Ser Glu Gln Gln Thr Phe 625 630 635 640

Arg Asp Leu Tyr Phe His Thr Glu Asp Arg Ser Pro Cys Ser His Lys 645 650 655

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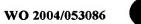
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Val Tyr Leu Arg Asp Pro His Gly Gly Lys His Arg Ser Asp Ile Asp

920

915

925



Arg Ala Ser Leu Pro Thr Gly Thr Glu Asn Lys Gln Ile Asn His Lys 930 935 940

Ile Leu Leu Pro Lys Gly Ser Met Gly Gly Thr Trp Met Leu Glu Glu 945 950 955 960

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Ser Asn Asp Ile Leu Asn Val Leu Ile Thr Tyr Ser Phe Thr Val Ser 50 55 60

Tyr Ile Phe Phe Met Ser Phe Lys Ile Leu Glu Ala Leu Leu Val Cys 70 75 80

Ile Ser Ile Leu Leu Thr Phe Gly Val Tyr Tyr Glu Lys Asn Lys
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Asn Met Ile Asp Ile Cys Thr His Phe Cys Ser Asn Pro Tyr Le $\hat{u}$  Ser 100 105 110

Ile Asn Asn Leu Asp His Met Asn Ile Ser Cys Leu Cys Lys Lys Gln 115 120 125

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Ser Met Lys Tyr Tyr Glu Ile Phe Tyr Leu Lys Lys Phe Leu Phe

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Thr	Met	Leu	Pro 180	Asn	Phe	Leu	Val	Glu 185	Tyr	Leu	Leu	Ile	Ser 190	Asp	Pro
Lÿs	Asn	Asp 195	Gly	Ile	Met	Val	Gly 200	Lys	Asn	Ile	Ser	Gly 205	Glu	Asp	Arg
Gly	Ile 210	Ile	Ser	Val	Ile	Phe 215	Cys	Asp	Ile	Asp	Asp 220	Phe	Gln	Asn	Met
Val 225	Ser	Thr	Leu	Gln	Pro 230	His	Val	Leu	Val	Glu 235	Thr	Ļeu	Asp	Asn	Leu 240
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Glu	Thr	Val	Phe 260	Glu	Ser	Tyr	Leu	Ala 265	Ala	Ser	Gly	Leu	Ser 270	Glu	Lys
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Lys	Ala	Ile	Ser 340		Val	Ile	Gly	Ser 345		Lys	Pro	Gln	Tyr 350		Leu
Phe	: Gly	Asp 355		Val	Asn	Thr	Ala 360		Arg	Met	Lys	Ser 365	Thr	Ser	Leu
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Asp 385		Thr	Phe	Ile	Trp 390		Glu	Arg	Lys	Val 395		Ile	Lys	Gly	Lys 400



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Arg Lys Gly Glu Ser Leu Asn Tyr Tyr Ser Ser Ser Asn Leu Leu 

Ser Gln Leu Gly Ser Glu Ala Val Ser Ile Tyr Glu Glu Arg Glu Asp 

Ile Lys Glu Gly Ser Met Asp Ile Ile Lys Glu Ser Ser Arg Asp Ile 

Ile Lys Glu Asp Ser Arg Asp Ile Ile Lys Glu Ile Ser Thr Asn Ile 

Ser Lys Ser Ser Ser Arg Asn Ile Ser Lys Ser Ser Ser Arg Ser Ile 

Ser Asp Ile Lys Glu Gly Gln Ile Ile Asp Lys Glu Asp Leu Ile Phe

Lys Ile Asn Arg Met Lys Asn Lys Ile Asp Ser Arg Tyr Ser Lys Arg 

Ile Asp Lys Glu Ser Arg Asp Lys Ile Ser Asp Lys Thr Asn His Val 

Leu Asp Glu Val Val Lys His Ser Asp Ile His Leu Leu Asn Tyr Glu 

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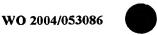
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Tyr Val Leu Glu Ser Pro Leu His Leu Ile Gly Asp Ile Val Asp Asn Asn Ile Lys Arg Lys Lys Lys Lys Glu Ile Lys Thr Ile Val Ser Asp Asp Met Phe Thr Ser Pro Val Asn Ile Lys Glu Tyr Asn Tyr Asn Glu Gln Glu Arg Lys Lys Glu Ile Val Gly Asn Leu Ser Tyr Asp Lys Thr Lys Lys Ile Phe Pro Phe Ile Lys Phe Thr Lys Glu Gly Arg Ile Lys Lys Lys Ile Glu Lys Lys Glu Lys Lys Glu Lys Lys Glu Asn Asn Asn Asn Phe Leu Tyr Asn Asp Asp Tyr Ser Ser Tyr Ser Ser Pro Lys Tyr Gly Asp Asn Glu Asn Asn Phe Val Ile Lys Tyr Ile Arg Glu Arg Lys Asp Phe Gln Lys Lys Phe Asp His Pro Asn Phe Asn Phe Ser Lys Phe Leu His Asn Tyr Asn Pro Met Lys Asn Lys Asn Lys Asn Lys Lys Asn Asn Lys Asn Val Arg Arg Asn Glu Tyr Pro Asn Tyr Thr Ser Ser Ser Lys Asp Gly Val Ser Tyr Asn Phe Leu Ser Asp Ser Leu Phe Ser Ser Asp Asn Glu Tyr Ser Ser Asp Asn Glu Tyr Ser Ser Asp Ser Glu Lys Tyr Tyr Lys Lys Arg Phe Lys Lys Asn Lys Lys Ile Ile Lys Phe Asp Asp Leu Phe Thr Lys Ile Tyr Ile Lys Lys Arg Leu Leu 



-- -- - ---

Gln Met Asn Asn Tyr Asp Val Lys Gly Lys Gly Lys Lys Leu Lys Asn 885 890 895

75

Lys Gly Met Glu Arg Asn Lys Thr Lys Tyr Lys Asn Val Asn Glu Ile 900 905 910

Thr Lys Met Lys Tyr Phe Val Asn Asn Glu Asn Arg Asp His Glu Val 915 920 925

Asn Lys Glu Asp Ile Ser Lys Ser Met Gln Lys Tyr Phe Leu His Ile 930 935 940

Ser Lys His Lys Lys Glu Gln Ile Glu Asp Lys Lys Lys Thr His Lys 945 950 955 960

Tyr Phe His Lys Asn Val Glu Cys Val Tyr Pro Tyr Ala Gly Asn Asn 965 970 975

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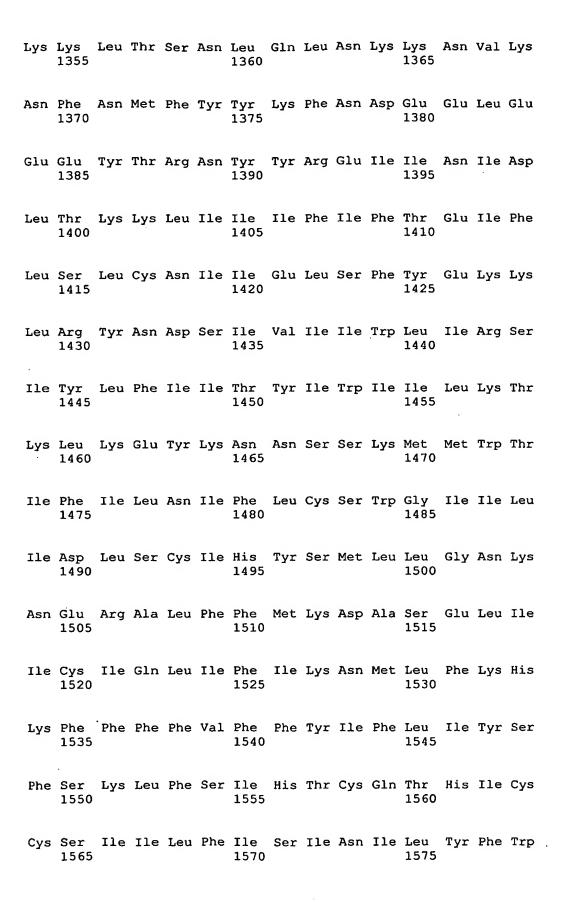
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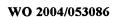
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Ser	Lys 1145	Asn	Lys	Gly	Lys	Asn 1150	Lys	Leu	Gly	Lys	Lys 1155	Ile	Ser	Phe	
Phe	Ser 1160	Met	Asn	Asn	Lys	Tyr 1165	His	Glu	Ser	Glu	Ile 1170	Met	Asn	Glu	
Glu	Asp 1175		Lys	Asn	Met	Leu 1180	Asn	Leu	Thr	Gln	Ser 1185	Gln	Ile	Ile	
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Lys	Phe 1235	_	Phe	His	Ser	Lys 1240	Asp	Ser	Asp	Asp	Ile 1245	Lys	Gly	Asn	
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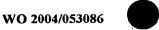
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- Ile Asn Lys Val Ile Ser Ser Lys Tyr Phe Phe Lys Asn Asp Asp Ile 35 40 45
- Cys Tyr Asn Lys Asn Asn Leu Asp Phe Lys Trp Tyr Leu Lys Lys Asp 50 55 60
- Arg Lys Lys Ser Arg Lys Ile Lys Lys Lys Gln Lys Lys Arg Lys Arg 65 70 75 80
- Lys Met Ile Met Met Lys Arg Gly Val Glu Asn Val Lys Asn Ala Asp 85 90 95
- Ser Ser Asn Asn Asp Val Cys His Asp Gln Asn Asn Asn Asn Phe Asn 100 105 110
- Asp Pro Leu Val Ser Lys Asn Thr Asn Tyr Asn Tyr Leu Tyr Thr Asn 115 120 125
- Asn Asn Glu Asn Asn Met Lys Glu Ser Thr Phe Leu Lys Ile Asp Glu 130 135 140
- Ser Tyr Leu Ser Thr Ser Tyr Ile Leu Asn Gly Lys Phe Val Ser Gly 145 150 155 160
- Asn Asn Ile Ser Asp Asn Lys Asn Asp Leu Asn Glu Lys Lys Tyr Ile 165 170 175
- Asn Ile Lys Arg Thr Asn Ser His Asn Asp Thr Ser Ser Leu Ser Ile 180 185 190
- Ser Gln Asn Asn Phe Ser Lys Ile Lys Lys Lys Gly Ala Ser Ser 195 200 205
- Ile Asn Ser Tyr Asp Glu Ser Ser Pro Asn Val Ser Pro Pro Ser Met 210 215 220



Tyr Ser Ser Glu Asn Leu Ser Tyr Asn Glu Lys Arg His Asn Asn Asn Ser Asp Asn Asn Asp Arg Asn Met Lys Ser Tyr Asn Tyr Ser Ser Ser Asn Ile Asn Lys Asn Cys Ser Ser Ser Ser Thr Ser Ser Ser Ile Ser Ser Ser Ser Ile Ser Ser Ser Ile Ile Ser Ser Ile Ile Ser Ser Ser Cys Ser Ser Val Thr Cys Ser Asp Ser Ser Leu Asn Ile Tyr Asn Thr Lys Arg Ser Ser His Gly Ser His Asn Gln Phe Cys Gly Ser Met Ser Cys Tyr Glu Lys Asp Lys Lys Asn Arg Leu Asp Asn Lys Asn Lys Met Lys Asn Lys Asn Ile Leu Asn Lys Lys Lys Tyr Lys Asn Lys Lys Met Pro Lys Thr Ile Asp Gly Asn Asp Thr Ser Leu Leu Leu Ser Ser Ser Thr Ser Ser Cys Asn Thr Lys Val Ser Phe Asp Asn Asn Glu Asn Tyr Gly Ile Ile Lys Glu Phe Ser Leu Cys Lys Ile Asn Leu Phe Ile Lys Glu Ala Lys Leu Leu Phe Phe Asn Lys Asn Ile Ser Ile Ser Asp Val Ser Leu Tyr Val Thr Thr Ile Met Glu Asp Lys Lys Tyr Ile Gly Lys Leu Arg Lys Leu Ser Ser Arg Thr Leu Pro Met Asn Asn Leu Ile Ile Asn Glu Tyr Ile Asn His Asn Ile Lys Asp Val



Tyr Thr Asp Ile Ile Ile Asn Ile Arg Tyr Lys Asn Arg Lys Lys Glu 475 470 465 Lys Glu Asp Ile Ile Leu Gly Arg Ala Ile Ile Pro Leu Phe Leu Ile 490 485 Leu Asn Thr Tyr Lys Trp Lys Ile Lys Lys Ile Lys Asn Lys Ile Arg 510 500 505 Tyr Cys Thr Lys Cys Phe Leu Trp Leu His Ile Phe Pro Cys Asn Asn 520 525 Lys Leu Phe Asn Tyr Lys Phe Phe Lys Pro Val Glu Gly Phe Glu Glu 530 540 Tyr Gly Met Leu Asn Pro Leu Tyr Thr Leu Gly Phe Leu Asn Ile Gln 560 555 Ile Lys Ile Ile Phe Lys Arg Asn Pro Leu Phe Leu Thr Phe Leu Ser 570 Asn Ile Arg Lys Pro Leu Phe Tyr Tyr Lys Leu Pro Val Gln Phe Glu 585 590 580 Pro Leu Tyr Cys Gln Tyr Tyr Ser Glu Asn Leu Tyr Val Tyr Ala Lys 600 Asn Ile Pro Leu Trp Ile Tyr Lys Phe Phe Tyr Ile Phe His Tyr Lys Arg Leu Glu Met Ile Ser Leu Asn Cys Tyr Asp Tyr Ile Cys Ile Leu 630 635 Ile Phe Trp Leu Phe Phe Phe Asp Leu Val Val Leu Ser Pro Phe Ser Leu Ile Phe Val His Leu Phe Phe Cys Ile Phe Phe Ile Ser Leu Ser 665 Tyr Lys Tyr Gly Lys Phe Val Pro Pro Tyr Tyr Lys Lys Lys Asn Leu

Phe Tyr Asn Phe Arg Pro Ile Arg Val Ser Arg Val Ser Arg Arg Asn



Cys Asp Tyr Thr Lys Arg Arg Ile Glu Thr Thr Asn Phe Ile Leu Asn 705 710 715 720

Asp Gln Lys Asn Val Glu Ile Tyr Asn Arg Glu Lys Lys Leu Asp Leu 725 730 735

Leu Asp Asp Asn Asn Val Asp Ala Asn Tyr Cys Lys Tyr Pro Tyr Cys 740 745 750

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Asn Lys Gly Val Asp Lys Asn Ile Ile Lys Gly Lys Asn Met Met Thr 770 775 780

Arg Gly Gly Gly Leu Asn Ile Tyr Asp Ala Cys Lys Met Phe Ile Lys 785 790 795 800

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Glu Asn Asn Asn Asp Val Asp Ser Val Glu Lys Thr Asp Ile Leu Leu 915 920 925

Asn Leu Ser Asn Gly Lys Asn Asn Gly Asn Val Thr Ser Ser Leu Cys 930 935 940



Glu Asn Leu Phe Val Tyr Asn Gln Asp Lys Ile Gln Arg Lys Lys 945 950 955 960

Val Pro Tyr Lys Asn Lys Glu Arg Asp Asn Lys Asp Asp Leu Asp Glu 965 970 975

Lys Lys Asp Met Tyr Ile Cys Asn Asp Asp Ser Ser Val Ile Thr Ser 980 985 990

Ser Glu Lys Gly Val Thr Lys Glu Arg Ile His Met Asn Lys Glu Lys 995 1000 1005

Leu Asn Tyr Asn Gly Ser Met Glu Cys Ser Ser Val Cys Val Glu 1010 1015 1020

Lys Asn Asn Met Ser Tyr Ile Ala Arg Arg Ile Gln Asn Met Met 1025 1030 1035

Tyr Asp Thr Lys Glu Lys Met Lys Leu Asp Gln Ile His Met Asn 1040 · 1045 1050

Lys His Met Ser Gly Phe Met Lys Leu Phe Asn Val Lys His Val 1055 1060 1065

Glu Asn Glu Lys Glu Asn Asp Ile Asp Lys Tyr His Asp Lys Gly 1070 1075 1080

Glu Ser Asp Lys Gln Val Pro Ser Ser Val Gly Ser Tyr Lys Leu 1085 1090 1095

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Lys Glu Glu Phe Asp Glu Lys Glu Glu Phe Asp Glu Glu Glu Glu 1115 1120 1125

Glu Gly Gly Gln Asp Glu Glu Ser Lys Lys Met Ser Arg Val Lys 1130 1135 1140

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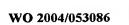




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Tyr Met Phe Ser Tyr Ile Pro Phe Val Phe Phe Arg Phe Leu Phe Phe Val Thr Cys Ser Tyr Phe Ile Ile Arg Ser Tyr Glu Leu Thr Glu Asp Gly Asn Arg Ala Cys Leu Tyr Tyr Lys Lys Arg Lys Ile Gln Phe Leu Lys Asn Arg Lys Ile Ser Leu Ala His Gly Leu Phe Glu Thr Tyr Lys Trp Lys Asn Ile Ile Lys Ile Ile Lys Lys Thr Leu Lys Lys Lys Asp Thr Asn Ile Phe Lys Tyr Ile Cys Leu Thr Cys Ala Phe Lys Ile Tyr Lys Leu Phe Lys Ile Ile Phe Glu Asn Ile Leu Leu Tyr Ile Leu Phe Ile Leu Phe Phe Ile Lys Asn Trp Tyr Thr Arg Leu Leu Ile Leu Lys Asp Ile Glu His Met Gln Ile Ala Lys Leu Gln Gly Phe Lys Asn Leu Tyr Phe Phe Ile His Asn Arg Ile Ile Lys Arg Glu Gln Lys Asn Val Met Ser Asn Thr Ser Ser Asn Glu Ile Asn Asn Arg Lys Ser Ser Val Ile Lys Ile Val Asn Ile Asp Asp Met Glu Lys Asn Glu Glu Asn Met Asn Lys Asn Asp Asn Asn His Asp Lys Asn Asp Asp Ile Val Asp Val Asn Asn Val His Met Asn Ile Asn Asn Asp Asn Met Asn Thr Asn Asn Glu 



86

Tyr Glu Ile Ile Lys Arg Arg Asn Gln Asn Asn Met Leu Asp Gly 1625 1630 1635

Lys Arg Lys Ser Val Lys Ser Leu Met Tyr Glu Asn Tyr Lys Asn 1640 1650

Leu Glu Ser Tyr Val Tyr Ser Ser Ser Asp Lys Glu Ala Val Ser 1655 1660 1665

Ile Ile Asn Glu Asp Asp Ile Ile Asp Glu Glu Glu Glu Gly 1670 1680

Asn His Gln Lys Glu Lys Leu Asn Lys Asp Asn Ile Asn Leu Asp 1685 1690 1695

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Leu His Tyr Tyr Phe Lys Lys Arg Lys Tyr Asp Leu Phe Asn Asn 1745 1750 1755

Phe Ile Asn Ile Asn Arg Asn His Met Tyr Thr Tyr Lys Asp Ile 1760 1765 1770

Asn Leu Phe Tyr Ser Asn Glu Asp Gln Lys Met Asn Asn Ile Asn 1775 1780 1785

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Asp Ser Asp Asn Asn Asn Gly Asp Asn Ser Asp Asp Asp Asp Asp 50 55 60

Lys Lys Tyr Lys Glu Glu Glu Glu Lys Ile Lys Lys Phe Ile Glu Ile 85 90 95

Lys Lys Asp Ile Asn Asn Ile Glu Ser Cys Tyr Met Leu Asn Met Phe 100 105 110

Lys Phe Asn Leu Glu Ser Phe Lys Met Tyr Leu Ile Asn Ile Ile Glu 115 120 125

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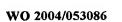
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Glu Glu Asn Tyr Gln Ile Lys Phe Ile Asn Asn Leu Glu Lys Lys Lys 225 230 235 240

Ser Ser Gly Gln Leu Tyr Asn Leu Asp Asp Ser Tyr Asn Lys Asn Leu 245 250 255



Leu Phe Thr Phe Asn Lys Leu Asn Val Met Lys Lys Lys Phe Val Ser 260 265 270

Phe Tyr Lys Phe Glu Val Glu Lys Lys Asn Leu Ile Leu Ser Lys Phe 275 280 285

Asn Glu Leu Ile Asn Leu Thr Lys His Val Glu Glu Glu Ile Gln Glu 290 295 300

Lys Lys Thr Thr Met Lys Asn Glu Leu Ile Asn Asn Ile Tyr Ser Phe 305 310 315 320

Lys Ile Asp Ile Lys Thr Phe Arg Glu His Phe Leu Lys Met Asn Phe 325 330 335

Lys Ser Glu His Ile Asn Pro Leu Asn Ala Phe Glu Leu Leu Lys Arg 340 345 350

Tyr Lys Glu Glu Ile Asn Met Leu Lys Asn Lys Tyr Asn Ser Tyr Tyr 355 360 365

Lys Gly Glu Ser Ile Phe Gly Leu Lys His Gln Thr His Ser Asp Leu 370 375 380

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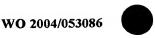
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Pro Ile Val Asp Glu Leu Glu Lys Lys Asn Ile Leu Lys Arg His Trp 465 470 475 480

Ile Glu Ile Ile Asn Ile Leu Lys Glu Lys Lys Lys Lys Asp Ile Thr 485 490 495



Gly Lys Glu Lys Lys Ile Gln Lys Lys Ser Tyr Ala Asp Glu Gln Lys 500 505 510

Asp His Pro Lys Asp Asn Ile Asn Asn Lys Ser Asn Asn Asn Lys Asn 515 520 525

Asn Asn Lys Asn Asn Asn Ile Asn Asn Asn Asn Gln Val Ile Asn 530 535 540

Glu Lys Val His Gln Ile Asp Pro Leu Val Asp Met Glu Lys Asn Asn 545 550 555 560

Val Leu Glu Asp Leu Asn Val Gln Gln Met Ser Asn Glu Asn Lys Asn 565 570 575

Val Lys Gln Val Glu Leu Ile Asn Asp Leu Glu His Gln Thr Asn Lys 580 585 590

Thr Ser Thr Gln Lys Asp Val Phe Glu Lys Asn Asp Asn Asp Asn 595 600 605

Asn Asp Lys Asn Asn Ile Asn Leu Ile His Gly Asp Thr Asp Glu Asn 610 620

Met Tyr Asn Thr Ser Glu Phe Glu Asp Glu Lys Met Lys Lys Lys Asn 625 630 635 640

Ile Glu Asn Lys Lys Arg Ile Asn Asp Gln Thr Asp Glu Glu Ile Ile 645 650 655

Ser Lys Lys Asp Ile Ser Phe Gln Asp Gly Gly Leu Leu Glu Glu Ser 660 665 670

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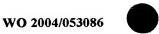
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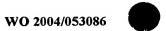
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- Ser Asn Ser Ser Gln Leu Phe Lys Thr Leu Asn Leu Lys Glu Phe Cys 995 1000 1005
- Asp Lys Asn Ile Ala Gln Val Ala Leu Ile Cys Leu Gln Val Met 1010 1015 1020
- Trp Thr Asn Asp Ile Glu Lys Cys Ile Tyr Lys Tyr His Ser Glu 1025 1030 1035
- Lys Asn Ile Leu Lys Val Thr Asn Lys Lys Ile Asn Tyr Ile Met 1040 1045 1050
- Ser Glu Leu Val Asn Ile Cys Leu Ser Asp Leu Gly Thr Lys Leu 1055 1060 1065
- Asn Arg Thr Lys Tyr Glu Thr Leu Val Thr Ile His Val His Gln 1070 1075 1080
- Arg Asp Leu Phe Thr Glu Ile Ser Ala Lys Ile Lys Glu His Lys 1085 1090 1095
- Ile Lys Thr Thr Thr Asp Phe Asp Trp Ile Lys Gln Thr Arg Ile 1100 1105 1110
- Tyr Tyr Lys Val Glu Lys Asn Ile Ile Leu Ile Ser Ile Ser Asp 1115 1120 1125
- Val Asp Phe Ile Tyr Ser Tyr Glu Tyr Leu Gly Ile Lys Glu Arg 1130 1135 1140
- Leu Cys Ile Thr Pro Leu Thr Asp Arg Cys Tyr Leu Thr Cys Ala 1145 1150 1155
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- Gly Ile Tyr Val Ile Val Thr Asn Cys Ser Asn Gln His Lys Tyr 1190 1195 1200
- Lys Asp Met Ala Lys Ile Phe Lys Gly Leu Cys Arg Ser Gly Leu 1205 1210 1215



Trp Gly Cys Phe Asp Glu Phe Asn Arg Ile Asn Leu Asp Val Leu Ser Val Val Ala Met Gln Ile Glu Ser Ile Val Thr Ala Lys Lys Gln Ser Leu Lys Tyr Phe Leu Phe Pro Gly Asp Ser Lys Ser Ile Asn Leu Asn Pro Ser Ser Ala Tyr Phe Ile Thr Met Asn Pro Gly Tyr Ala Gly Arg Gln Leu Leu Pro Glu Asn Leu Lys Ile Phe Phe Arg Phe Ile Ser Met Met Val Pro Asp Arg Gln Ile Ile Ile Lys Val Lys Leu Ala Ser Val Gly Tyr Leu Asp Ile Asp Asn Leu Ser Asn Lys Phe Lys Ser Leu Tyr Asn Leu Cys Glu Glu Gln Leu Ser Lys Gln Lys His Tyr Asp Phe Gly Leu Arg Asn Ile Leu Ser Val Leu Arg Thr Ala Gly Asp Thr Lys Arg Ser Ala Gly Pro Asn Glu Asn Asp Glu Glu Met Leu Leu Met Arg Thr Leu Arg Asp Met Asn Leu Ser Lys Leu Ile His Asp Asp Val Leu Leu Phe Leu Ser Leu Leu Asn Asp Val Phe Pro Lys Phe His Asn Ile Thr Lys Lys Ser Phe Gln Leu Ile Glu Glu Asn Val Leu Gln Ile Ile Lys Lys Lys Leu Cys Ala Lys Gly Lys Trp Ile Leu Lys Ile Leu Gln Leu 





- Tyr Glu Thr Ser Leu Val Arg His Gly Phe Met Leu Val Gly Asn 1445 1450 1455
- Thr Leu Thr Gly Lys Thr Glu Ile Leu Asn Ile Leu Thr Ser Ala 1460 1465 1470
- Leu Thr Asn Ile Gly Ser Val Thr Lys Ile Ile Thr Leu Asn Pro 1475 1480 1485
- Lys Ala Ile Thr Ser Glu His Met Tyr Gly Val Lys Asp Asn Leu 1490 1495 1500
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- Gly Pro Val Asp Ala Ile Trp Ile Glu Asn Leu Asn Thr Val Leu 1535 1540 1545
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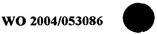


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Leu Tyr Thr Glu Glu Asn Glu Lys Ile Lys Gln Gln Gln Pro Lys

	1895					1900				•	1905			
Lys	Lys 1910	Lys	Glu	Leu	Gln	Pro 1915	Lys	Gly	Asp	Tyr	Asn 1920	Asp	Туr	Val
Ser	Thr 1925	Lys	Gln	Asn		Glu 1930	Glu	Asp	Lys	Asn	Asn 1935	Ile	Glu	Leu
Asp	Asn 1940	Glu	·Gln·	Asn	Val	Glu 1945		Gly	Glu	Glu	Phe 1950	Glu	Asn	Glu
Ile	Ser 1955	Leu	Ile	Туr	Asp	Phe 1960		Phe	Asp	Met	Lys 1965	Leu	Lys	Lys
Leu	Val 1970	Lys	Trp	Asn	Val	Gly 1975	Pro	Phe	Lys	Met	Pro 1980	Arg	Asn	Ile
Asn	Ser 1985	Ile	Ser	Ser	Ile	Leu 1990	Ile	Pro	Thr	Ile	Glu 1995	Thr.	Thr	Lys
Val	Glu 2000		Ile	Ile		Leu 2005		Ser	Asn	Ile	Pro 2010	Ile	Arg	Cys
Tyr	Asn 2015		His	Thr	Tyr	Lys 2020		Thr	Leu	Leu	Leu 2025	Gly	Ser	Thr
Gly	Ser 2030		Lys	Thr	Ser	Ile 2035		Leu	Leu	Tyr	Thr 2040	Ser	Lys	Gln
Glu	Lys 2045		Thr	Lys	Arg	Phe 2050			Ser		Val 2055	Thr	Thr	Pro
Glu	Lys 2060	Phe	Gln	Leu	Phe	Ile 2065	Glu	Ser	Glu	Leu	Glu 2070	Arg	Lys	Thr
Gly	Lys 2075		Tyr	Gly	Pro	Ile 2080	Gly	Asn	Thr	Lys	Ser 2085	Ile	Ile	Phe
Ile	Asp 2090		Met	Ser	Met	Pro 2095	Lys	Ile	Asn	Glu	Trp 2100	Gly	Asp	Gln
Ser	Thr 2105		Glu	Leu	Leu	Arg 2110		Leu	Ile	Glu	Phe 2115	Gln	Gly	Phe
Tyr	Phe 2120		Asp	Lys	Asp	Lys 2125	Arg	Gly	Asn	Phe	Lys 2130	Lys	Ile	Ile

Asp	Leu 2135	Glu	Tyr	Ile	Gly	Cys 2140	Ile	Asn	His	Pro	Gly 2145	Суѕ	Gly	Asn
Asn	Asp 2150	Ile	Pro	Lys	Arg	Leu 2155	Lys	Ser	Lys	Trp	Phe 2160	Asn	Val	Asn
Ile	Leu 2165	Pro	Туг	Asn	Leu	Asn 2170	Ser	Ile	Asn	Thr	Ile 2175	Tyr	Gly	Thr
Val	Leu 2180	Arg	Thr	Lys		Asn 2185	Lys	Lys	Gln	Asn	Phe 2190	Ser	Asp	Glu
Ile	Ile 2195	Glu	Asn	Ile	Asp	Lys 2200	Val	Ile	Leu	Cys	Thr 2205	Ile	Asn	Leu
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His	Tyr 2225		Tyr	Thr	Thr	Arg 2230	Asp	Leu	Ala	Lys	Ile 2235	Phe	Tyr	Ser
Met	Leu 2240		Cys	Pro		Glu 2245	Ser	Ile	_		Asn 2250	Leu	Tyr	Asn
Phe	Leu 2255		Leu	Trp		His 2260	Glu	Суз	Glu	Arg	Val 2265	Leu	Ile	Asp
Lys	Leu 2270		Arg	Met	Glu	Asp 2275	_	Thr	Phe	Ser	Leu 2280	Asp	Gln	Leu
Lys	Gln 2285	Ile	Phe	Asn	Gln	Tyr 2290	Tyr	Pro	Ser	Tyr	Lys 2295	Asp	Ile	Cys
Glu	Lys 2300		Ile	Tyr	Phe	Ser 2305	Tyr	Phe	Tyr	Val	Ser 2310	Glu	Lys	Glu
Gln	Gln 2315		Tyr	Met	Ile	Glu 2320	Asn	Asp	Leu	Ile	Glu 2325	Asn	Asn	Thr
Thr	Gln 2330		Lys	Thr	Glu	Asn 2335	Asn	Lys	Ile	Asn	Ile 2340	Thr	Ile	Ser
Pro	Ser 2345	_	Ile	Asn	Asp	Thr 2350	Ser	Asn	Asn	Leu	Ile 2355	Ser	Thr	Lys



Leu Asp Asn Thr Asn Glu Leu Asn Glu Lys Ile Asp Asp Thr Lys Thr Arg Ser Asn Ser Ala Leu Tyr Arg Arg Asn Asp Val Asp Asn Gln Asn Ile Ile Asn Asn Asn Ile Leu Thr Lys Glu Gly Asp Asn Asn Gly Asp Ile Asp Asn Ile Asn Thr Phe Ser Phe Ser Trp Met Lys Lys Asp Tyr Lys Ile Val Val Asp Phe Glu Arg Leu Arg Tyr Ile Val Tyr Glu Tyr Met Lys Glu Tyr Asn Ile Asn Asn Val Lys Lys Leu Asp Leu Val Phe Phe Asp Asp Ser Leu Lys His Leu Ile Ile Ile Asn Arg Val Met Gln Thr Pro Asn Gly Ser Cys Met Leu Val Gly Val Gly Gly Ser Gly Lys Arg Ser Leu Thr Lys Leu Ser Val Phe Ile Ser Glu Gln Val Leu Phe Gln Leu Asn Ile Thr Lys Thr Tyr Thr Lys Asn Leu Phe Phe Glu Asp Leu Lys Ser Leu Tyr Ile Ser Ala Gly Gln Met Asn Lys Lys Thr Thr Phe Leu Leu Ser Asp Ser Asp Ile Glu Lys Asn Asp Phe Ile Leu Glu His Val Asn Ser Ile Leu Ser Thr Gly Leu Val Tyr Gly Leu Phe Ile Lys Asp Glu Lys Glu Ala Ile Cys Ala Glu Met Lys Glu Ser Tyr Leu 



- Lys Glu Met Asn Lys Ser Asn Gln Ser Ser Lys Ile Lys Gly Gly 2585 2590 2595
- Lys Lys Lys Asn Lys Asn Asp Tyr Asn Asn Ile Asp Asp Met 2600 2605 2610
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- His Lys Glu Phe Ala Leu Arg Tyr Gln Gln Phe Pro Cys Ile Tyr 2690 2695 2700
- Asn Cys Val Thr Ile Asn Trp Phe Leu Lys Trp Pro Leu Glu Ala 2705 2710 2715
- Leu Val Asn Val Ser Thr Ala Tyr Leu Asn Asn Phe Asn Ile Asp 2720 2730
- Ile Glu Asp Asn Leu Lys Asp Asp Phe Phe Asn Leu Phe Ala Ile 2735 2740 2745
- Val His Asn Lys Val Ser Asp Thr Cys Asp Thr Tyr Lys Glu Arg 2750 2760
- Met Arg Arg Asn Thr Tyr Val Thr Pro Lys Ser Tyr Leu Ser Phe 2765 2770 2775
- Ile Asp Leu Tyr Lys Gln Met Tyr Val Lys Lys Tyr Asp Glu Ile 2780 2785 2790
- Lys Cys Leu Lys Glu Ser Val Asp Ile Gly Leu Lys Lys Leu Asn 2795 2800 2805
- Glu Ala Ala Met Asp Val Gln Lys Met Arg Glu Ser Leu Thr Ser

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Val	Glu 2855	Val	Ser	Lys		Arg 2860	Asp	Lys	Cys	Ile	Lys 2865	Glu	Lys	Asp
Leu	Ile 2870	Leu	Lys	Asp	Gln	Glu 2875	Glu	Ala	Asp	Lys	Asp 2880	Leu	Lys	Ala
Ala	Leu 2885	Pro	Tyr	Leu		Glu 2890		Glu	Glu	Ala	Ile 2895		Ser	Ile
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Gly	Lys 2930		Lys	Glu	Pro	Lys 2935		Asp	Val	Lys	Tyr 2940	Val	Asn	Lys
Gln	His 2945		Asp	Phe	Ile	Gln 2950		Ser	Phe	Asp	Glu 2955	Tyr	Ala	Lys
Pro	Leu 2960		Ala	Asp	Ile	Arg 2965		Leu	Asn	Leu	Leu 2970	Phe	Asp	Phe
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Leu	Lys 2990	1				2995					Thr 3000			
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Ala	Met 3020	)				3025	•				val 3030	•		
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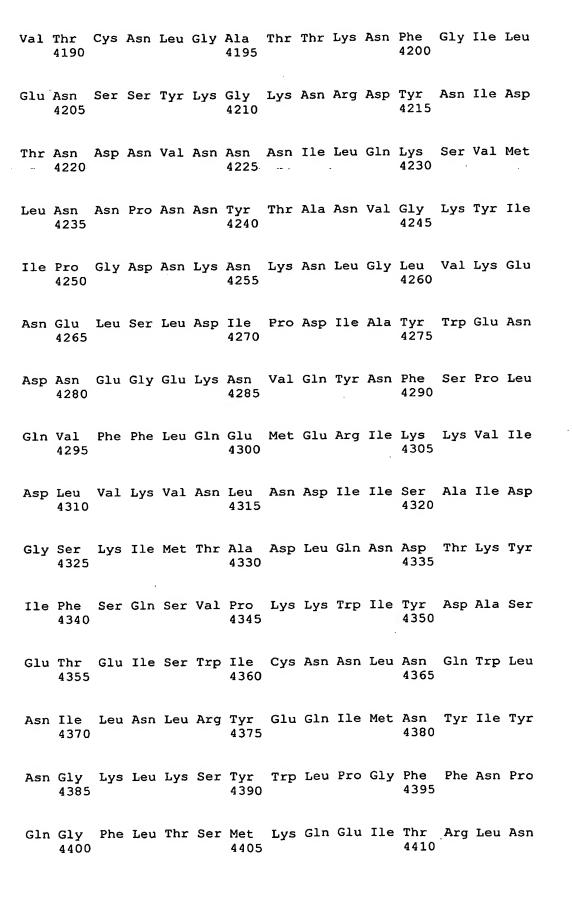
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Asp	Ile 3530		Phe	Phe		Asn 3535		Leu	Ser	His	Tyr 3540	Ser	Pro	Ser
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Val	Ile 3590	Asn	Asn	Thr	Met	Asp 3595	Ser	Ser	Ser	Met	Asn 3600	Asn	Asp	Thr
Met	Asn 3605		Tyr	Leu	Gly	Thr 3610	Asn	Glu	Asn	Asp	Lys 3615	Asn	Lys	Lys
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	Asn 3650					Asn 3655						_	Gly	Asn
Ser	Ser 3665	Asn	Asn	Ala	Gly	Asp 3670	Ile	Asn	Ser	Cys	Lys 3675	Asn	Asn	Thr
Ser	Val 3680		Asp	His	Asn	Ile 3685	Ser	Asn	Lys	Asn	Lys 3690	Ile	Asp	Leu
His	Lys 3695	_	Gly	Ala	Gly	Lys 3700	Gly	Lys	Ile	Ser	Ser 3705	Thr	Lys	Trp
Leu	Phe 3710		Asn	Glu	Lys	Leu 3715	Tyr	Lys	Asn	Ile	Ile 3720	Ser	Leu	Ser



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Ile	Leu 3740	Asn	Val	Ile	Gln	Leu 3745	Asn	Glu	Asn	Thr	Trp 3750	Lys	Asn	Tyr
Tyr	Asp 3755		Leu	Asp	Ile	Glu 3760	Asn	Lys	Asn	Ile	Pro 3765	Tyr	Tyr	Asn
Glu	Arg 3770	Leu	Asp	Val	Asn	Ser 3775	Gln	Ile	Ser	Ser	Phe 3780	Ile	Lys	Leu
Cys	Leu 3785	Ile	Arg	Суѕ	Leu	Arg 3790	Glu	Asp	Arg	Thr	Ile 3795	Leu	Cys	Ala
Asn	Lys 3800		Val	Asp	Glu	Val 3805	Leu	Asn	Arg	Asn	Ser 3810	Asp	Thr	Ile
Lys	His 3815	Glu	Thr	Leu	Glu	Asn 3820	Ile	Phe	Ser	Glu	Ser 3825	Ser	Asn	Arg
Lys	Pro 3830		Leu	Phe	Leu	Leu 3835	Ser	Leu	Ala	Ser	Asp 3840	Pro	Thr	Asn
Met	Ile 3845		Asp	Phe	Ala	Lys 3850	Lys	Phe	Lys	Lys	Tyr 3855	Pro	Thr	Asp
Lys	Ile 3860		Met	Gly	Glu	Gly 3865		Glu	Val	Ile	Ala 3870	Lys	Glu	Lys
						Ser 3880							Gln	Asn
Cys	His 3890		Asn	Lys	Asn	Phe 3895		Ile	Asp	Val	Tyr 3900	Asn	Met	Leu
Lys	Asn 3905		Asn	Glu	Ile	Glu 3910		Asp	Phe	Arg	Leu 3915		Leu	Thr
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Ile	Lys 3935		Ser	Thr	Ser	Leu 3940		Ser	Gly	Ile	Lys 3945		Asn	Met
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Lys Lys Asp Gln Leu Ser Leu Asp Glu Val Val Leu Tyr Thr Asp 4420

Ile Lys Asn Tyr Asp Val Glu Lys Ile Lys Glu Phe Pro Glu His 4435 4430

Gly Phe Asn Ile His Gly Leu Phe Ile Glu Gly Ser Lys Trp Asn 4450

Trp Gln Glu Gly Lys Leu Glu Glu Ser Ser Pro Lys Ile Leu Cys 4465 4460

Glu Asn Met Pro Val Ile His Ile Thr Val Val Ser Asn Lys Asp 4480 4475

Lys Lys Ile Lys Phe Ile Glu Asn Asn Lys His Met Phe Tyr Asn 4495 4490

Cys Pro Val Tyr Lys Tyr Asn Val Arg Thr Asp Lys Tyr Phe Ile 4505 4510

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Asn Tyr Ser Lys Asn Asn Tyr Gly Leu Asn Asp Gln Glu Leu Arg Ala 40

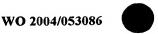
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Thr Asn Asn Gly Asp Leu Lys Tyr Asn Asn Asp Leu Ile Lys Glu Gly

Glu Asn Lys Arg Asn Asn Lys Leu Asn Asn Tyr Lys Phe Asn Met Asn Lys Val Asn Asp Asn Lys Asn Phe Asn Lys Tyr Thr Glu Ile Tyr Asn -Lys-Glu Ser Glu-Pro Glu Lys Gln Asn Asn Ser Asn Asn Asn Leu Gly Ile Pro Thr Leu Ile Lys Lys Glu Val His Ile Lys Asn His Asn Thr Phe Ser Ser Asn Gly Lys Ile Leu Glu Asn Lys Asp Ile Asp Lys Met Ser Asp Thr Ser Lys Lys Asn Asp Arg Asn Phe Arg Ser Asn Asp Ile Lys Asn Phe Lys Asn Asn Asp Thr Lys Asn Asn Ala Thr Leu Ser Glu Asp Asn Lys Asn Arg Tyr Asn Ile Thr Thr Asn Lys Asn Asn Glu Lys Lys Glu Tyr Asn Met Lys Lys Ser Asn Glu Asn Glu Tyr Ala Phe Asn Thr Glu Lys Thr Asn Val Asn Asn Asp Ala Leu Lys Glu Glu Arg Asn Asn Tyr Lys Tyr Leu Asn Asn Gln Thr Asp Val Asn Ile Asn Asn Leu Gln Glu Arg Asp Ile Asn Leu Tyr Asn Lys Asn Glu Ser Asp Lys Lys Leu Glu Gln Ser Phe Arg Glu Glu Asp Ile Lys Asn Ala Tyr Leu Pro Glu Asn Lys Asn Phe Gln Lys Thr Leu Thr Asn Asn Glu Lys Asn Glu Asp Asn Lys Ile Pro His Ile Asp Pro Ser Asn Asn Glu Leu Asp Lys 



Lys Gly Asn Tyr Asn Lys Tyr Glu Ile Gly Lys Ile Lys Lys Asn Asn Glu Glu Asn Lys Gln Asn Val Thr Val Glu Glu Asn Ile Asn Pro Glu Lys Ile Arg Lys Asp His Glu Gln Asn Ile Gln Tyr Ser Lys Asn Asp Pro Ile Thr Asp Ile Gln Asn Ser Thr Asn Ala Val Leu Lys Lys Ile Lys Pro Thr Glu Phe Glu Asn Tyr Thr Lys Glu Glu Leu Gln Asn Val 625· Ser Ser Ser Glu Val Arg Asp Asp Asn Leu Asn Glu Ile Asn Arg Lys Gly Glu Thr Asn Met Phe Ser Glu Lys Ser Thr Leu Lys Lys Gly Glu Asn Asp Trp Asn Glu Tyr Glu Tyr Phe Lys Leu Lys Ser Asn Glu Leu Lys Val Leu Gly Ile Ile Asn Lys Tyr Ser Pro Lys Gly Gly Phe Ser Ile Ser Val Asn Cys Gly Gly Tyr Asp Asp Phe Arg Glu Ile Pro Gly Ile Ser Asn Leu Leu Arg His Ala Ile Phe Tyr Lys Ser Glu Lys Arg Ile Thr Thr Leu Leu Ser Glu Leu Gly Lys Tyr Ser Ser Glu Asn Asn Ser Arg Ile Gly Glu Ser Phe Thr Thr Tyr Tyr Ala Ile Gly Lys Ser Glu Asn Ile Tyr Asn Ile Leu Thr Leu Phe Ser Gln Asn Leu Phe Tyr 

Pro Leu Phe Asp Glu Asp Phe Ile Glu Asn Glu Val Arg Glu Ile Asn

Asn Lys Tyr Ile Ser Met Glu Asn Asn Ser Leu Asn Cys Leu Lys Ile 805 810 815

Ile Ser Gln Phe Ile Thr Asp Leu Lys Tyr Ser Lys Phe Phe His 820 825 830

Gly Asn Tyr Ile Thr Leu Cys Asn Asn Val Leu Lys Asn Gly Leu Asn 835 840 845

Ile Lys Lys Leu Leu Tyr Asn Phe His Lys Lys Cys Tyr Gln Pro Lys 850 855 860

Asn Met Ala Leu Thr Ile Leu Leu Gly Lys Lys Gly Asn Ser His Asp 865 870 875 880

Asn Tyr Asn Met Asn Asp Ile Glu Asn Phe Val Ile Asp Ile Phe Glu 885 890 895

Lys Ile Lys Asn Tyr Asp Tyr Val Asn Glu Ser Asn Asn Lys Arg Gln 900 905 910

Lys Glu Lys His Ile Val Asn Phe Lys Asp Asp Thr Phe Asn Ile Glu 915 920 925

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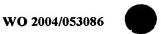
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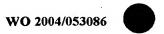
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Lys Phe Ile Ser Glu Glu Asn Lys His Ile Phe Lys Ser Asn Ile Leu Tyr Asn Ile Pro Cys Leu Ile Lys Ser Ser Tyr Gly Tyr Asn Ile Tyr Phe Lys Arg Gly Leu Thr His Ile Ser Lys Val Lys Thr Asp Phe Ile Phe Tyr Phe Pro Ser Glu Lys Phe Thr Phe Tyr Glu Ser Val Phe Thr Arg Ile His Ile Ile Ile Leu Gln Lys Lys Ile Glu Arg Phe Leu Ser Asp Tyr Thr Thr Cys Ser Val Asn Ala Asn Ile Met His Asp Ala Ile Ser Tyr Thr Leu Ser Ile Glu Ser Asn Gly Tyr Phe Phe Glu Glu Phe Phe Asn Lys Ile Gln Glu Leu Leu Ser Leu Lys Glu Ile Pro Ser Arg Asp Glu Tyr Asn Glu Ala Tyr Asp Glu Leu Asn Ile Ile Ile Gln Thr Asp Thr Thr Ser Gly Val Asp Lys Ser Leu Lys Ile Met Tyr Ser Leu Phe Asn Lys Tyr Thr Pro Thr Asn Lys Glu Met Tyr Asp Ile Leu Asn Ala Tyr Phe Phe Tyr Pro Ser Tyr Asn Ala Tyr Arg Thr Tyr Val Asn Glu Tyr Phe Leu Arg Asn Tyr Val Val Ile Phe Ile Tyr Gly Asn Ile Ile Ile Ser Asp Leu Lys Gly Glu Glu Asn Ile Thr Lys Asn Asn Asn Asn 



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Glu Ser Cys Asp Glu Glu Met Ser Lys Asp Asn Phe Gln Ile Phe 1955 1960 1965

Tyr Asn Phe Thr Asn Asp Ile Asn Lys Ile Arg Glu Tyr Phe Arg 1970 1975 1980

Gly Lys Phe Thr Asn Asp Lys Glu Val Lys Glu Asn Cys Ser Ile 1985 1990 1995

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- Ser His Asn Asn Asn Ser His Asn Asn Asn Asn Lys Ala Glu Asn Ser 225 230 235 240
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- His Arg Asn Ser Gln Ser Ile Ile Tyr Asn Ile Asn Asp Glu Tyr Asn 260 265 270
- Glu Lys Ile Lys Lys Asn Lys Lys Gln Asp Tyr Ser Asn Tyr Ile Thr 275 280 285
- Tyr Glu Asn Phe Glu Lys Ile Val Leu Ser Ile Asn Asp Ile Lys Arg 290 295 300
- Gln Leu Leu Gly Thr Gly Asp Glu Ile Ile Thr Ser Gln Ile Lys Tyr 305 310 315 320
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- Asn Phe Glu Cys Tyr Lys Lys Ala Leu Lys Cys Asn Glu Phe Leu Lys 340 345 350
- Leu Leu Gly Ile His Thr Lys Val Ala Asp Val Phe Leu Gln His Glu
- Leu Leu Lys Arg Lys Asp Lys Asn Lys Thr Lys Asn Gly Thr Met Arg

Asn Arg Lys Lys Tyr Lys Asn Asp Ser Asn Arg Ile Ala Asn His Leu Ile Ile Lys Ser Phe Ser Glu Ser Thr Asn Thr Arg Gly Ser Ile Ile Asn Asp Ser Thr Ser Phe Leu Phe Leu Arg Lys Gln Lys Glu Lys Lys Ala Ile Leu Tyr Glu Arg Lys Ser Thr Phe Ser Ser Met Glu Asn Lys Ser Gln Asn Lys Ser Gln Asn Lys Ser His Asn Lys Asn Ile Lys Ser Val Ser Arg Ile Leu Ser Arg Val Asn Lys Leu Ser Ser Thr Glu Leu Ile Pro Asn Glu Cys Asp His Lys Pro Asn Glu Glu Val Lys Ser Thr Ser Asp Val Leu Thr Pro Ile Phe Phe Asn Asn Gly Asp Glu Lys Met Asn His Asp Thr Asp Gly Asn Met Val Tyr His Lys Asn Asn Val Asp Asp Asn Leu Val Asp Gly Asp Val Val Ser Gln Gly Lys Arg Cys Ser Phe Phe Ser Ser Cys Glu Asn Lys Lys Asn Glu Glu Asn Lys Ser Ile Thr Phe Asn Asp Ile Asn Ser Gly Asn Ile Asn Thr Asn Ser Cys Ile Met Asn Asn Met Ile Val Thr Lys Glu Ser Asn Glu Glu Ile Ile Asn Glu Glu Ala Gln Ser Ser Tyr Ile Tyr Asn Lys Asn Ile Phe Cys Ser Lys Tyr

Asn Thr Lys Lys Asp Lys Asn Glu Pro Leu Lys Cys Asp Leu Phe Glu

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Phe Lys Lys Cys Ile Glu Lys Tyr Lys Glu Tyr Val Asn Gln Gly Glu 885 890 895

Gly His Leu Lys Asp Glu Glu Glu Glu Lys Asn Asp Asp Glu Glu Glu 900 905 910

Gly Glu Asp Gly Glu Asp Asp Glu Glu Glu Asn Asp Asp Asp Asp Asp 915 920 925

Asp Glu Asp Gly Asp Asp Asp Glu Asp Gly Asp Asp Asp Asp Asp 930 935 940

Asn Asp Asp Asn 945 950 955 960

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Asn Asp Asp Gly Ile Asn Cys Cys Thr Asn Leu Phe Lys Asp Asp 995 1000 1005

Asp Thr Leu Ser Ala Leu Glu Lys Asn Val Thr Asn Asn Asn Leu 1010 1015 1020

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Tyr Lys Asp Phe Met Lys Asn Asn Thr Thr Leu Phe Ser His Phe 1040 1045 1050

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Lys Asp Val Leu Asn Tyr Arg Pro Lys His Asn Asn Asp Ile Asn 1070 1075 1080

Tyr Tyr Asn Ile Pro Cys Glu Asp Gln Ile Lys Ser Asp Glu Lys 1085 1090 1095 Lys Ser Leu Leu Asn Val Glu Phe Gly Asp Asp Ile Ile Lys Lys Lys Phe Phe Ile Ser Ser Val Asn Ser His Tyr Val Met Ile Asn Asn Asn Leu Thr Lys Glu Gln Met Leu Tyr Leu Ile Arg Asn Ile Leu Met Ser Ile Glu Asp Tyr Leu Lys Lys Glu Lys Asn Arg Asp Tyr Asn Lys Ile Phe Phe Leu Phe Phe Ser Ile Phe Ile Tyr Asn Thr Gln Asn Gly Gly Asp Gln Lys Glu Met His Glu Asp Glu Lys Trp Asp His Thr Asn Ile Asn Glu Asp Lys Asn Val Glu Lys Asn Asp Asp Tyr Lys Asn Leu Ser Asn Asn Glu Asn Ser Val Tyr Tyr Asn Thr Met Leu Arg Glu Ser Leu Trp Asn Lys Lys Lys Tyr Ile Lys Leu Asn Ile Phe Lys Asn Ile Ile Leu Val Ile Ser Ile Val Arg Tyr Phe Leu His Thr Ile Thr Ile Ser Gln Lys Tyr Thr Ser Ser Tyr Asp Ser Leu Asp Asp Ser Asn Met Ile Lys Ser Met Asn Ser Leu Lys Leu Asn Glu Ile Asn Ile Leu Leu Asn Arg Ala Ser Glu Ile Leu Glu Lys Tyr Ser Leu Gly Ser Val Glu Asn Lys Lys Val Tyr Ile Asn Lys Ser Asn Tyr Tyr Asn Ser Ser Lys Lys Gly Lys Leu Ser Val Ser Leu Arg Gln Asn Lys Gln Lys Lys Thr Phe

His Arg Ile Leu Ala Val Tyr Phe Gly His Glu Arg Trp Asp Leu 1345

Val Met Asn Met Met Ile Gly Ile Arg Ile Ser Ser Ile Lys Lys 1360 1355

Phe Ser Ile Asn Asp Ile Ser Asn Tyr Phe His His Lys Asp Val 1380 1370 1375

Ile Gln Leu Pro Thr Ser Asn Ala Gln His Lys Val Ile Phe Lys 1395 1385 1390

Asn Tyr Ala Pro Ile Ile Phe Lys Asn Ile Arg Asn Phe Tyr Gly 1405 1410

Ile Lys Ser Lys Glu Tyr Leu Thr Ser Val Gly Pro Glu Gln Val 1420 1425

Ile Ser Asn Met Val Leu Gly Asn Leu Ser Thr Leu Ser Glu Leu 1430 1435 1440

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Tyr Asn Gly Gly Glu Ile Met Gln Pro Asn Ser Lys Leu Cys Glu Leu

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Asp His Thr Ile Asp Thr Asn Val Thr Asp Gly His Ser Asn Pro Cys

Glu Gly Arg Gln Thr Val Arg Phe Pro Asp Asp Asn Arg Ser Gln Cys Thr Lys Asn Arg Ile Lys Asp Ser Val Asp Asn Ser Val Gly Ala Cys Ala Pro Tyr Arg Arg Leu His Leu Cys Ser His Asn Leu Glu Ser Ile Gln Thr Asn Asn Tyr Asp Ser Ser Lys Ala Lys His Asn Leu Leu Ala Glu Val Cys Tyr Ala Ala Lys Phe Glu Gly Glu Ser Ile Val Lys Asn Tyr Glu Gln Leu Gly His His Thr Thr Glu Gly Ile Cys Thr Ala Leu Ala Arg Ser Phe Ala Asp Ile Gly Asp Ile Ile Arg Gly Lys Asp Leu Tyr Leu Gly Asn Pro Gln Glu Ser Ala Arg Arg Lys Gln Leu Glu Asp Asn Leu Arg Lys Ile Phe Glu Lys Ile Tyr Lys Glu Leu Thr Ser Ser Arg Asn Gly Lys Thr Asn Gly Ala Glu Glu Arg Tyr Lys Asp Gly Ser 

260 265 270

Phe Arg Asn Thr Cys Ser Asn Gly Glu Lys Pro Thr Gly Glu Lys Cys 275 280 285

Gln Cys Ile Asp Gly Thr Val Pro Thr Asn Leu Asp Tyr Val Pro Gln

Gly Asn Tyr Tyr Lys Leu Arg Glu Asp Trp Trp Asn Ala Asn Arg Leu

Asp Ile Trp Lys Ala Met Ile Cys Lys Ala Pro Gly Asn Ala Pro Tyr

Tyr Leu Arg Trp Phe Glu Glu Trp Ala Glu Glu Phe Cys Arg Lys Arg Asn Leu Lys Leu Gln Asn Ala Ile Lys Asn Cys Arg Gly Met Asp Asp Asp Gly Lys Glu Lys Tyr Cys Ser Arg Asn Gly Tyr Asp Cys Thr Lys Thr Ile Arg Ser Ile Asp Lys Tyr Ser Met Asn Arg Glu Cys Thr Lys Cys Leu Tyr Val Cys Asp Pro Tyr Val Lys Trp Ile Asp Asn Lys Lys Lys Glu Phe Glu Lys Gln Lys Lys Lys Cys Glu Asn Glu Ile Tyr Arg Asn Asn Glu Ser Ser Gln Asn Ser Pro Lys Asn Tyr Asn Asn Met Tyr Glu Thr Asp Phe Tyr Gly Asn Leu Lys Lys Asp Tyr Gln Ser Met Asn Asp Phe Leu Lys Leu Leu Asn Ser Glu Thr Pro Cys Thr Asn Ile Ile Asp Ala Lys Ser Lys Ile Asp Phe Thr Lys Asp Pro Glu Glu Thr Phe Ser His Thr Glu Tyr Cys Asp Pro Cys Pro Trp Cys Gly Leu Lys Thr Gln Ala Asp Gly Thr Trp Lys Arg Leu Tyr Glu Asn Asp Pro Gln Cys Pro Ile Lys Pro Lys Tyr Glu Pro Pro Lys Gly Val Glu Pro Thr Glu Thr Asp Val Leu Tyr Thr Gly Lys Glu Asn Lys Asp Ile Ile Val Lys Leu Arg Glu Phe Cys Lys Thr Asp Gly Asn Thr Gly Phe Lys Asn Glu 

Glu Trp Asn Cys Tyr Tyr Gln Val Gly Asn Asp Lys Cys Val Leu Glu 545 550 555 560

Asn Gly Glu Glu Leu Gly Gly Glu Lys Lys Val Lys Asp Tyr Asp Asn 565 570 575

Phe Leu Met Phe Trp Val Ala His Met Leu Lys Asp Ser Ile Glu Trp 580 585 590

Arg Ser Lys Leu Ser Asn Cys Leu Lys Ser Asp Lys Lys Thr Cys Ile 595 600 605

Thr Thr Cys Asn Asp Asn Cys Gln Cys Tyr Asp Lys Trp Ile Gly Lys 610 620

Lys Lys Val His Trp Thr Gln Ile Lys Lys His Phe Asp Lys Gln Thr 625 630 635 640

Asp Phe Gln Gly Trp Gly His Tyr Phe Val Leu Glu Thr Val Leu Glu 645 650 655

Gly Asp Gln Phe Phe Thr Asp Ile Thr Lys Ala Tyr Gly Asp Ala Arg
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Glu Ile Val His Ile Gln Glu Met Leu Gln Lys Lys Glu Gln Val 675 680 685

Leu His Glu Asp Ala Ser Asn Met Lys Thr Ile Ile Asp Glu Leu Leu 690 695 700

Asp His Glu Leu Lys Glu Ala Lys Gln Cys Ile Val Asn His Lys Asp 705 710 715 720

Asn Asn Cys Pro Ala Asp Leu Ser Asp Ser Glu Asp Glu Glu Glu Asp
725 730 735

Ile Pro Gln Arg Gln Asn Lys Cys Ala Lys Pro Ser Gly Thr His Ile 740 745 750

Arg Ala Leu Val Asn Lys Val Ala Ser Asn Met His His Lys Lys 755 760 765

Arg Gln Leu Val Asn Arg Gly Val Ser Ser Lys Leu Lys Gly Asp Ala
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Ala Lys Gly Glu Tyr Arg Lys Ser Gly Thr Thr Ile Lys Leu Lys Asp

785 790 795 800

Ile Cys Ser Ile Thr Asp Asp His Ser Asn Ala Lys Arg Gly His Thr 805 810 815

Asp Gln Pro Cys Lys Arg Lys Asp Ser Lys Val Asn Val Lys Asn Arg 820 825 830

Arg-Trp Met Asp Thr Ala-Gly Phe Ile-Ser Asn Thr Tyr Lys Asp Ile 835 840 845

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Leu Gln Thr Thr Asn Lys Leu Leu Asn Gly Asn Asp Ile Asn Gly Asn 865 870 875 880

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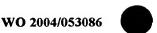
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Lys Gln Tyr Gly Glu Leu Val Ser Ala Ser Asn Gly Cys Lys Asp Glu Arg Val Lys Val Val Arg Ile Arg Val His Asn Val Gln Arg -- Ala-Cys Lys His Val Lys Ile Ile Lys Asn Leu Leu Ile His Gly Lys Glu Gln Trp Asp Lys Met Glu Ile Lys Tyr Lys Leu Leu Tyr Leu Gln Ala Gln Thr Thr Ala Ala Asn Gly Gly Pro Asp Thr Tyr Ser Gly Leu Val Asp Glu Asn Glu Lys Pro Val Val Asn Phe Leu Phe Glu Leu Tyr Lys Glu Asn Gly Gly Lys Ile Gly Asn Pro Arg Asp Thr Pro Arg Ala Lys Arg Ser Lys Arg Glu Thr Ala Pro Ala Ser Val Ala Lys Asn Asp Val Tyr Ser Thr Ala Ala Gly Tyr Val 1160 1165 1170 His Gln Glu Met Gly Pro His Met Glu Cys Lys Thr Gln Thr Glu Phe Cys Glu Lys Thr Asp Glu Gln Tyr Asn Glu Asn Tyr Thr Phe Lys Asn Pro Pro Pro Gln Tyr Lys Asp Ala Cys Ile Cys Asn Thr Arg Pro Pro Pro Lys Glu Asp Ser Arg Lys Arg Ser Glu Asp Ser Asp Glu Glu Glu Lys Val Lys Glu Thr Lys Val Glu Glu Lys Ala Thr Glu Asp Ala Val Asp Thr Gly Pro Pro Pro Ala Pro Lys Glu



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1480

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Glu	Ala 1835	Cys	Lys	Asn	Ala	Asn 1840	Ile	Phe	Lys	Gly	Ile 1845	Lys	Glu	Asn
Lys	Trp 1850	_	Cys	Val	Tyr	Phe 1855	Cys	Lys	Ser	Asp	Val 1860	Cys	Gly	Leu
Lys	Lys 1865		Asn	Asp	Ile	Asp 1870		Asn			Ile 1875	Leu	Ile	Arg
Ala	Leu 1880	Phe	Lys	Arg	Trp	Leu 1885	Glu	Tyr	Phe	Leu	Asp 1890	Asp	Tyr	Asn
Lys	Ile 1895	Arg	Lys	Lys	Leu	Asn 1900	Pro	Cys	Ile	Asn	Asn 1905	Gly	Glu	Lys
Ala	Ile 1910	Cys	Thr	Asn	Gly	Cys 1915	Val	Glu	Gln	Trp	Ile 1920	Asn	His	Lys
Arg	Thr 1925	Glu	Trp	Thr	Asn	Leu 1930	Lys	Ser	Phe	Asn	Glu 1935	Gln	Tyr	Asn

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Gly	Leu 1970	Val	Lys	Leu		1975		Val	Lys	Cys	Asn 1980	Cys	Gly	Asn
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Cys	Leu 2000		Gln	Lys	Leu	Glu 2005		Lys	Ala	Glu	Lys 2010	Суѕ	Lys	Asp
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Asn Val Tyr Ser Gly Ile Asp Leu Ile Asn Asp Thr Leu Ser Gly

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Gln	Cys 2465	Lys	Asn	Asp	Asn	Glu 2470	Arg	Leu	Ala	Lys	Leu 2475		Glu	Leu
Trp	Glu 2480		Glu	Thr	Gln	Cys 2485	Gly	Asp	Ile	Asn	Ser 2490	_	Ile	Pro
Ser	Gly 2495	Lys	Leu	Ser	Asp	Thr 2500	Pro	Ser	Asp	Asn	Asn 2505	Ile	His	Ser
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Pro	Ser 2525	Asp	Asn	Asn	Ile	His 2530	Ser	Asp	Ile	Pro	Tyr 2535	Val	Leu	Asn
Thr	Asp 2540	Val	Ser	Ile	Gln	Ile 2545	His	Met	Asp		Pro 2550		Pro	Ile
Asn	Glu 2555	Phe	Thr	Tyr	Val	Asp 2560	Ser	Asn	Pro	Asn	Gln 2565	Val	Asp	Asp
Thr	Tyr 2570	Val	Asp	Ser	Asn	Pro 2575	Asp	Asn	Ser	Ser	Met 2580	Asp	Thr	Ile
Leu	Asp 2585	Asp	Leu	Glu	Lys	Tyr 2590	Asn	Glu	Pro	Tyr	Tyr 2595	Asp	Val	Gln
Asp	Ile 2600	Tyr	Asn	Asp	Val	Asn 2605	Asp	Asp	Asn	Asp	Ile 2610	Ser	Thr	Val
Asp	Thr	Asn	Ala	Met	Asp	Val	Pro	Ser	Lys	Val	Gln	Ile	Glu	Met

2620

2625

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Asn Ile Asp Leu Asn Ile Tyr Pro Asn Met Ser Asn Tyr Val Asp Ile 35 40 45

Gly Ser Asn Ile Tyr Val Glu Gln Ile Lys Asn Ile Ser Lys Glu Glu 50 55 60

Val Thr Lys Lys Lys Ser Ile Leu Asn Ser Lys Tyr Ile Ser Ser Lys 65 70 75 80

Asn Asn Glu Phe Val Val Ala Gln Leu Tyr Glu Leu Asn Asn Tyr Asn 85 90 95

Glu Asn Asn Ile Tyr Glu Asp Arg Asn Leu Phe Ser Asn Ser Thr Asn 100 105 110

Ile Tyr Ser Asn Asp Asn Asn Met Lys Lys Tyr Leu Ile Gln Lys Cys 115 120 125

Gly Lys Lys Asn Ile Lys Lys Arg Met Asp Ile Leu Asn Gln Glu Asn 130 135 140

Asn Asn Met Gly Ile His Lys Asn Ile Val Tyr Asp Asp Asn Asn Asn 145 150 155 160

Asn Lys Asn Val Thr Tyr Asp Asp Asn Asn Lys Asn Val Thr Tyr Asp 165 170 175

Asn Asn Asn Lys Asn Val Thr Tyr Asp Asn Asn Lys Asn Val Thr 180 185 Tyr Asp Asn Asn Asn Lys Asn Val Thr Tyr Asp Asn Asn Asn Lys Asn 200 Val Thr Tyr Asp Asn Asn Asn Asn Ser Cys Ser Ile Ile Lys Tyr 215 Glu Leu Arg Lys Thr Ser Ile Cys Lys Tyr Trp Ile Lys Gly Ile Cys 235 230 Ala Asn Val Glu Cys Asn Phe Ala His Gly Glu His Glu Leu Lys Tyr Thr Phe Gly Val Tyr Lys Thr Thr Ile Cys Lys His Trp Lys Lys Asn Gly Met Cys Ser Ser Gly Ile His Cys Arg His Ala His Gly Glu Ser 280 Glu Leu Gln Pro Lys Asn Leu Pro Leu His Leu Leu Lys Lys Lys Asn Asn Leu Lys Asn Lys Asn Gln Thr Lys Ser Phe His Thr Asn Lys Glu 305 Leu Thr Ile Asn Glu Tyr Asn Asp Arg Ser Ala Asn Asn Arg Asn Val 330 Glu His Met Tyr Lys Asn Lys Val Asp Pro Leu Lys Asn Asn Asn Asn 340 345 Asn Asn Asp Asn Ile Tyr Tyr Gly Asn Glu Glu Asn Gln Lys Asp 355 360 Val Asn Ile Phe Arg Met Asp Thr Phe Tyr Asn Asn Ile Phe Asp Ser 375 380 370 Arg Asn His Met Asp Lys Pro Pro Pro His Asn Ile Asn Asn Asn Asn 385 390 395 Ser Asn Asn Asn Asn Asn Asn Ile Val Ser Val Glu Gly Lys Pro 405 410 415

WO 2004/053086

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Tyr Gln Ile Cys Lys Asp Asp Asn Asn Leu Leu Asn Asn Asn Glu Lys 465 470 475 480

Thr Phe Phe Phe Ser Asn Val Asn Asn Lys Met Val Glu Cys
485 490 495

Asn Asn Met Asn Asn Ile Phe Asn Asp Ile His Lys Lys Glu Asn Thr 500 505 510

Ile Thr Leu Asn Asn Asn Ser Asn Asn Val Ile Asn Ile Lys Lys Asn 515 520 525

Ile Ile Asp Asp Ala Asp Ile Ser Lys Val Thr Asn Val His Ile Tyr 530 535 540

Lys Asp Asp His Leu Lys Asn Thr Pro Ile Asn Asn Lys Lys Glu 545 550 555 560

Thr Arg Leu Ser Gln Gly Lys Lys Asn Thr Tyr Leu Lys Val Asn Phe 565 570 575

Phe Asn Asn Lys Asn Lys Asp Asn Asn Tyr Asn Asn Ile Ile Val 580 585 590

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Asp Asp Val Tyr Asn Gly Asn Met Asp Asn His Asn His His Val Asn. 705 710 715 720

Asn Asn Asn Thr Leu Cys Asn Thr Ser Leu Ser Asp Leu Cys Ser Asn 725 730 735

Asn Ser Ser Glu Ser Lys Lys Gln Glu Ala Val Cys Leu Asn Lys Asn 740 745 750

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Tyr Pro Trp Lys Glu Asn Lys Phe Lys Asn Val Asp Met Leu Asn Ile 900 905 910

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- Tyr Asn Tyr Asn Tyr Asn Tyr Asn Tyr Asn Tyr Ala Tyr Asp Asn 1115 1120 1125
- Ile Glu Leu Ser Asn Lys Asn Met Lys Asp Val Ile Asn Leu Tyr 1130 1135 1140



Thr Tyr Val Val Asn Lys Lys Asn Glu Lys Asn Ile Tyr Thr Ser 1145 1150 1155 Thr Asn Asn Ile Ile Cys Asn Asp Glu Tyr Ile Lys Lys Glu Asp Cys Gly Asp Cys Gln Met Val Glu Ser Thr Gln Met Phe Asp Glu Glu Ile Asn Cys Ser Pro Glu Asn Lys Ser Asn Asn Asn Asn Ile Asn Ser Asn Asn Ile Asn Ile Asn Ser Ser Ser Ser Asn Asn Asn Asn Asn Asn Asn Tyr Tyr Tyr Asn Asp Tyr His Asp Asp Asp Asn Asn Asn Ile Met Asn His Ser Tyr Tyr Asn His Ile Asn Asp Ser Tyr Tyr Tyr Gln Phe Asn Asp Leu His Ser Lys Glu Asn Gln Gln Lys Tyr Thr Tyr Asn Ile Asn Asn Leu Ile His Asn Met Lys Leu Leu Asn Thr Glu Tyr Glu Ser Pro Leu Asn Ser Glu Gln Glu Lys Thr Ile Leu Lys Asn Ile Ala Val Asp Arg Asn Asn Asn Ile Asn Ile Asn Asn Ile Thr Leu Pro Thr Leu Gln Asp 1310 1315 1320 Asn Gln Met Asn Asn Tyr Lys Lys Tyr Thr Asn Asp Leu Gly Ser Val Ser Glu Gly Tyr Thr Ser Thr Tyr Asn Asp Thr Leu Lys Met His Ser Glu Thr Phe Met Asp Ser Gln Asn Gly Met Tyr Ile Leu 

Pro Gln Tyr Val Thr Arg Glu Cys Ile Asn Ser Pro Tyr Asp Ser Ser Leu Phe Thr Asp Glu Asn Arg Glu Glu Lys Lys Asp Asn Lys Glu Arg Glu Ile Ile Gly Asn Met Leu Tyr Asp Glu His Ile Cys Met Asp Asp Glu Asp Leu Phe Gly Arg Ser His Leu Phe Asn Ile Phe Asn Asn Glu Glu Glu Ile Asp Ile Asn Gln Lys Asp Asn Tyr Tyr Asp Arg Asp Asp His Asn Asp Tyr His Arg Asp Asp His Asn Asp Tyr Asp Arg Asp Asp His Asn Asp Tyr Asp Arg Asp Asp His Asn Asn Tyr His Arg Asp Asp His Asn Asn His His Arg Asp Asp Asn Asn His His Arg Asp Asp His Asn Asn His His Arg Asp Asp Asn Asn Asn His His Gly Asp Asp Val Ile Tyr Glu Glu Thr Lys Lys Thr Asp Asn Ile Glu Ile Pro Leu Lys Asp Asn Asp Ile 1520 1525 Met Ile Asn Asn Ser Tyr Asn Asp Ser Leu Ile Asn Tyr Asn Lys Tyr Phe Val Lys Glu His Glu Tyr Asn Asn Ile Asn Asn Asn Asn Lys Ile Glu Glu Asn Leu Lys Ile Lys Asn Ser Tyr Asp Thr Ser Ser Lys Gln Asn Tyr Lys Glu Asn Asn Met Phe His Asp Val Asp Asn Phe Thr Ser Leu Leu Leu His Ile Asn Asn Tyr Asn Glu Lys •

1595 1600 . 1605

Asp Phe Met Asn Phe Lys Asn Glu Asp Tyr Thr Leu Asn Lys Glu 1610 1620

Ile Tyr Phe Asn Glu Cys Lys Tyr Val Lys Glu Ile Lys Asn Ile 1625 1630 1635

Asp-Gln Asp-Asn Thr Lys-Glu Leu Gly Ile Val Leu Gln Asn Asp

Asp Gln Ile Ser Glu Ser Asp Met Arg Thr Lys Lys Met Ile Tyr 1655 1660 1665

Ser Ile Phe Ile Lys Glu Glu Glu Thr Lys Lys Asn Lys Asn Leu 1670 1680

Glu Asn Ile Cys Tyr Thr Asn Glu Glu Glu Lys Tyr Asn Asn Leu 1685 1690 1695

Ser Ile Ile Asn Gln Lys Gln Asn Ile Thr Met Asp Ile Ile Lys 1700 1705 1710

Asn Val Asp Glu Leu Ser Phe Asp Asn Met Glu Gln Met Asn Ile 1715 1720 1725

Lys Ile Asn Asp Asn Gln Met Tyr Asn Glu Gln Val Met Asp Asn 1730 1740

Met Glu Asp Arg Ile Glu Lys Ile Asn Ile Leu Thr Asn Asp Asn 1745 1750 1755

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Lys Gln Ser Leu Lys Asp Asn Asn 1775 1780

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Glu Asn Tyr Leu Asn Ala Leu Thr Asp Asp Thr Met Asn Glu Thr Val 35 40 45

Phe Leu Asp Tyr Val Lys Gly Lys Met Met Asp Val Tyr Lys Glu Thr 50 55 60

Asn Met Asn Arg Tyr Asn Val Ile Asn His Ile Tyr Leu Thr Ser Lys 70 75 80

Val Trp Asp Thr Tyr Asn Tyr Leu Thr Pro Thr Leu Lys Val Lys Arg 85 90 95

Phe Arg Val Phe Lys Asp Tyr Ser Phe Phe Ile Asp Glu Val Lys Lys 100 105 110

Ile Tyr Glu Asn Lys Leu Lys Lys Ser Thr Ile Cys Asn Lys Ala Ile 115 120 125

Leu Ile Asn Arg Asn Lys Asn Val Glu Met Lys Lys Gly Leu Asn Asp 130 135 140

Lys Asn Glu Thr Ser Glu Lys Lys Val Glu Glu Asn Ile Lys Asn Arg 145 150 155 160

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Ile Ser Ile Phe Cys Asn Leu Arg Arg Asn Val Phe Ser Asn Phe Asn

40

45

Arg Asn Asp Leu Ile Asp Gln Asn Ile Val Tyr Leu Asn Val Cys Asn 50 55 60

Asn Glu Thr Tyr Tyr Asn Lys Ala His Glu Glu Asn Asp Lys Val Lys 65 70 75 80

Gly Tyr Ile Tyr Glu Glu Gly Leu His Asp Asn Met Phe Phe Ser Phe 85 90 95

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Met Gly Arg Arg Tyr Ser Tyr Asn Asp Asn Ile Glu Glu Leu Lys Lys 20 25 30

Leu Lys Lys Ile Leu Leu Asn Leu Asp Val Leu Ile Asp Val Ser Lys 35 40 45

Ile Val Ile Gln Lys Asn Glu Asn Phe Asp Met Glu Leu Leu Asn Asn 50 55 60

Val Asn Asp Arg Phe Val Glu Lys Ile Tyr Tyr Leu Leu Lys Asp Lys 65 70 75 80

Lys Lys Asn Met Leu Pro Glu Glu Glu Leu Val Glu Phe Ile Phe Leu 85 90 95

Leu Leu Lys Glu Arg Asn Glu Tyr Asn Asn Leu Glu Lys Lys Lys
100 105 110

Asn Ile Tyr Ile Asn Val Gln Lys Asn Leu Thr Asn Cys Pro Ile Lys 115 120 125

Asn Glu Val Thr Thr Leu Ile Gln Lys Ile Asn Lys Phe Tyr Tyr 130 135 140

Phe Lys Glu Phe Leu Leu Lys Glu Lys Tyr Asn Thr Lys Asp Asp Ala 145 150 155 160 Asn Lys Lys Tyr His His Asn Lys Glu Asp Thr Asn Asn Tyr Asn Asn



165 170 Ile Pro Glu Asn Tyr Lys Asn Gln Ser Lys His Asn His Asp Tyr Leu 180 Asn Tyr His Lys Asp Asn Ile Ile Asn Ile Asp Ile Asn Asp Leu Gly 200 Tyr Asn Asn Asn Asp Asn Asn Lys Glu Ser Val Phe Tyr Asn Lys Glu Ile Ile Lys Asn Asn Lys Gln Arg Asn His Phe Gln Gly Lys Glu Lys 230 Lys Asn Thr Lys Asp Glu Val Ala Thr Thr Ile His Asn Ile Leu Ser 250 Cys Lys Asp Ile Ser Ser Asn Gln Phe Asn Asn Tyr Asn Asn Thr Leu 260 265 Gln Thr Ser Asp Tyr Asn Lys Asp Phe Leu Tyr Lys Asp Val Leu Met 280 Asp Ile Met Ser Thr Asp Ser Glu Lys Asn Met Thr Ser Gln Lys Ser 295 Ile Thr Ser Glu Lys Asn Met Thr Cys Glu Lys Asn Met Thr Cys Glu 305 310 Lys Asn Ile Thr Cys Glu Lys Asn Ile Thr Cys Glu Lys Asn Ile Thr 325 330

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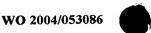
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Ile Glu Pro Leu Ile Ser Ser Tyr Ser Glu Tyr Ile Met Arg Asp Glu 405 410 415

144

Pro Thr Tyr Ile Pro Asp Lys Leu Leu Ser Glu Glu Asn Lys
420 425 .430

Lys Leu Glu Lys Glu His Cys His Met Lys Asn Asn Ile Lys His Asn 435 440 445

Asp Ile Ala His Val Thr Asn Asn Asp Ser Ile Asn Asn Tyr Leu Tyr 450 455 460

Asn Lys Tyr Tyr Ile Asn Glu Asp Asn Lys Ile Met Gln Asn Asp Ser 465 470 475 480

Asn Leu Asn His Asn Lys Asn Glu Asp Ile Lys Lys Val Asp Ile Glu 485 490 495

Asn Thr His Met Ile Asn Gly Tyr Asp Pro Asn Glu Asp Ile Leu Trp 500 505 510

Asn Asn Asn Lys Thr Ile Ser Ser Glu Lys Leu Cys Val Pro Arg Thr 515 520 525

Lys Asp Asn Glu Ile Leu Lys Asn Lys Glu Leu Asn Asn Tyr Leu Gly 530 535 540

Glu Ala Tyr Asn Asp Cys Ile Asn Glu Glu Thr Tyr Lys Asn Met Lys 545 550 555 560

Leu Glu Asn Cys Asp Glu Lys Lys Lys Thr Asn Phe Gln Asn Val 565 570 575

Asn Ser Asn Phe Lys Glu Gln His Leu Leu Phe Cys Asn Asn Leu Gln 580 585 590

Glu Gln Met Lys Tyr Arg Ser Asp Lys Asn Leu Lys Tyr Asp Glu Lys 595 600 605

Asn Asn Asn Thr Asn Asp Asp Ile Lys Ile Val Lys Pro Asn Asn Gln 625 630 635

His His Ile His Asn Asn Leu Leu His Tyr Ile Asn Asn Lys His Asn

650

655

- Leu Leu Asn Ser Ile Thr Leu Ser Asn Ser Leu Pro Gln Lys Asn Asp 660 665 670
- Tyr Gln Ile Asn Asn Phe Ile His Lys Asn Asp Thr Asn Glu Phe Lys 675 680 685
- Asn\_Leu Thr Ile Asn Asn Phe\_Gln Lys Lys Glu Lys Glu Leu Tyr Thr
  690 695 700
  - Leu Asn His Met Asn Thr Ile Lys Ser Asn Ile Asn Asn Ile His Met 705 710 715 720
  - Lys Asp Ser Gly Asp Thr Glu Val Thr His Asn Asn Gln Ser Phe Phe 725 730 735
  - Phe Asn Thr Asn Gln Ile Glu Asn Glu Lys Lys Lys Asn Asn Asn 740 745 750
  - Asn Asn Ile Lys Thr His Ile Ala Asn Phe Asn Ile Ile His Lys Asn 755 760 765
  - Asn Leu Asn Glu Ser Gly Lys Asn Met Glu His Tyr Ile Ala Ser Gln 770 780
  - Glu Glu Asn Ile Leu Phe Glu Asn Lys Asn Asn Asp Met Glu Glu Leu 785 790 795 800
  - Tyr Arg Glu His Ser Arg Glu Leu Leu Glu Glu Asn Ile Ile Asn Lys 805 810 815
  - Ile Gly Asn Asn Thr Lys Lys Lys Glu Tyr Asp Glu Cys Thr Met 820 825 830
  - Ser Thr Cys Ile Asp Asn Val Val Tyr Asn Ser His Asp Asn Ile Asn 835 840 845
  - Gly Glu Lys Lys Asp Glu Asn Asn Met Glu Tyr Phe Ile Lys Ser Glu 850 855 860
  - Asp Glu Ser Leu Lys Asp Phe Asp Met Leu Leu Tyr Asn Asn Arg Lys 865 870 875
  - Glu Asn Ser Glu Arg Glu Glu Asp Lys Ser Ile Glu Asn Ile Lys Met 885 890 895



Leu Gly Thr Glu Ser Phe Tyr Glu Asp Glu Asn Asn Asp Glu Asp Ile
900 905 910

Lys Gln Phe Asp Glu Asn Leu Thr Tyr Glu Gln Arg Lys Ile Asn Asp 915 920 925

Asp Asn Tyr Gly Asp Met His Tyr Ile Asp Val Glu Asp Asp Asp Tyr 930 935 940

Glu Asn Val Arg Asn Lys Asn Glu Asp Ser Ser Asn Ile Tyr Asp Asp 945 950 955 960

Glu Glu Ile Tyr Asn Gln Lys Glu Glu His Asp Gly Lys Lys Ile Phe 965 970 975

Leu Asn Arg Ile Glu Asn Asn Ala Ile Asn Asn Leu Tyr Lys Thr Tyr 980 985 990

Glu Met Ile Gln Gly Asp Asn Asp Asp Met Asp Asp Asn Tyr Tyr Leu 995 1000 1005

Tyr Asp Glu Asn Glu Lys Gly Ala Thr Lys Asn Ile Leu Cys Glu 1010 1015 1020

Phe Asn Lys Cly Lys Cly Ile Val Asn Lys Phe Asn Arg 1025 1030 1035

Asp Met Leu Gln Lys Ile Glu Lys Asn Tyr Asp Asn Asn Asp Ile 1040 1045 1050

Asn Gln Lys Lys Phe Met Asn Thr Arg Asn Asp Asn Tyr Ile Asn 1085 1095

Asn Asn Ile Tyr Leu Asn Lys Ala Asn Pro Asn Ile Phe Asn Glu 1100 1105 1110

Asn Thr Thr Asn Tyr Asn Gln Lys Glu Asn Ser Phe Asn Gln Ser 1115 1120 1125



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Lys	Lys 1145	Trp	Leu	Cys	Lys	Ile 1150	Asn	Ala	Arg	Glu	Lys 1155	Glu	Lys	Glu
Lys	Lys 1160				Lys	Lys 1165				Tyr	Asp 1170	Arg	Glu	Leu
Lys	Asn 1175		Thr	Phe	His	Pro 1180		Leu	Asn	Asn	Asn 1185	Arg	Ile	Lys
Arg	Glu 1190		Thr	Ile	Lys	Glu 1195	Met	Asn	Asp	Thr	Tyr 1200	Asp	Asp	Asp
Asp	Asn 1205		Asn	Leu	Ser	Glu 1210		Tyr	Asp	Cys	Tyr 1215		Lys	Tyr
Val	Asn 1220		Thr	Tyr	Tyr	Gly 1225	Asp	Asn	Asn	Lys	Asp 1230	Суз	Tyr	Asn
Phe	Asp 1235		Glu	Lys	Ile	Tyr 1240		Phe	Asn	Asn	Asn 1245	Ser	Tyr	Tyr
Lys	Asn 1250		Glu	Gln	Asn	His 1255	Ser	Phe	His	His	Phe 1260	Asn	Ile	Asp
Lys	Lys 1265		Asn	Asp	Asn	Thr 1270		Met	Lys	Lys	Lys 1275	Met	Asn	Arg
	Lys 1280			_		_	_		_		-		Leu	Leu
Leu	Gln 1295	Lys	Lys	Ile	Asp	Tyr 1300	Gln	Asn	Glu	Glu	Glu 1305	Lys	Lys	Phe
Lys	Lys 1310	Glu	Cys	Ile	Phe	His 1315	Pro	Thr	Ile	Lys	Asp 1320	Asn	Val	Lys
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- Leu Gln Tyr Arg Ile Pro His Met Asn Asn Gly Asn Ile Gln 1355 1360 1365
  - Asn Glu Lys Lys Asn Glu Gly Lys Gln Asn Asn Lys Lys Lys Thr 1370 1375 1380
  - Asn Asn Ile Pro Gln Pro Phe Ser Phe Asp Lys Gly Gln Tyr Lys 1385 1390 1395
  - Val Lys Ile Lys Pro Val Phe Phe Glu Arg Lys Ile Lys Ile Ser 1400 1405 1410
  - Glu Asn Lys Ile Ala Cys Leu Ala Val Arg Glu Asp Glu Asp Pro 1415 1420 1425
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  - Gln Glu Ser Phe Glu Lys 1460